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CUTANEOUS TUBERCULOSIS IN THE NEGRO: A CLINICAL ENTITY

REPORT OF TWO CASES (ONE ASSOCIATED WITH SYPHILIS)

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Many dermatoses assume an appearance in the Negro at variance with that in the white man. This is due to the Negro's greater tendency to hyperpigmentation and fibrosis and to different immunologic conditions. The difference in cutaneous manifestations is particularly noticeable in cutaneous tuberculosis. The difference in immunobiologic conditions is seen in the greater susceptibility of the Negro to tuberculosis in general, as shown by Dublin [1] and Opie [2] and by the mortality statistics of the United States Department of Commerce.[3] It has been corroborated by Pinner and Kasper,[4] who observed in a series of 500 autopsies that hematogenous metastases, exclusive of miliary tuberculosis, occur twice as often in the Negro as in the white man. The latter finding seems to be confirmed by a form of generalized tuberculosis of the skin in the Negro, cases of which have been reported frequently in the literature and presented before dermatologic societies in recent years. These cases resemble each other in morphologic characteristics and course, and one is forced to think of this eruption as a clinical entity occurring only in the Negro.

The purposes of this paper are to add two more cases of the same condition to those reported in the literature, to emphasize the clinical

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1. Dublin, L. I.: Health Gains Among Colored People, Statistical Bulletin, New York, Metropolitan Life Insurance Co., 1928, vol. 9.

2. Opie, Eugene L.: Epidemiology of Tuberculosis of Negroes, Nat. Tuberc. A. Tr. **26**:243, 1930.

3. Mortality Statistics in the Birth Registration Area, 1931-1932, United States Department of Commerce, Bureau of the Census, 1932.

4. Pinner, M., and Kasper, J. A.: Pathologic Peculiarities of Tuberculosis in the American Negro, Am. Rev. Tuberc. **26**:463 (Nov.) 1932. Klauder, Joseph V., in discussion of cases presented by Fox and Maloney.[5]

entity of the eruption and to attempt to clarify its nature. An additional feature of one of these cases, namely, the association of tuberculosis with syphilis, will also be discussed.

REPORT OF CASES

CASE 1.—A. R., a Negress aged 28, born in the United States, came under our observation on Jan. 23, 1934. She had been apparently well until the previous six months, had been married eleven years and had no living children. Nine years previously she had had two miscarriages, one after three months and one after four and one-half months of pregnancy. She had lived with a brother who died of pulmonary tuberculosis.

About one year previously her husband had a penile sore, which healed after a short time. The Wassermann reaction of his blood was negative. Six months later the Wassermann reaction of the patient's blood was found to be strongly positive. She then received antisyphilitic treatment with neoarsphenamine and a bismuth preparation.

Shortly after institution of this treatment an eruption appeared at the inner canthi of both eyes, at the nostrils and at the vermilion borders of the lips. It soon became generalized and increased in extent in spite of continuous antisyphilitic treatment, amounting to forty-eight injections of a bismuth preparation and neoarsphenamine.

General examination disclosed an apparently normal heart and lungs, but at the time of re-examination, two months later, bean-sized submaxillary glands were palpable.

The eruption was generalized, roughly symmetrical and rather sparse. On the forehead and at the inner canthus of each eye, extending to the bridge of the nose and to the upper and lower eyelids, there were ovoid, slightly raised plaques with a scarred and uneven center and a slightly raised border. On the vermilion border of the lips, the chin, the nostrils, the forehead and the cheeks there were discrete firm and elevated nodules, ranging in size from that of a pinhead to that of a split pea, some of which had slightly depressed centers (figs. 1 and 2). On the trunk and the extremities there were plaques ranging in size from that of a dime to that of a half dollar, oval, round or irregular, depigmented and atrophic in the center and hyperpigmented at the border. On the back of the neck and in the antecubital areas there were raised firm linear lesions, which showed hyperpigmentation at the borders (fig. 3). In the crural region the lesions were somewhat macerated.

The eruption thus consisted of three types of lesions. The tiny nodules at the vermilion borders of the lips, on the alae nasi and on the chin presented the picture of lupus miliaris disseminatus seen frequently in these locations in Negroes; the oval, round or irregular flat plaques suggested lupus erythematosus, and the linear lesions on the back of the neck and in the antecubital fossae looked like keloids.

Laboratory Examination.—The Wassermann test of the blood showed a 3 plus reaction. Several Wassermann tests performed later were all anticomplementary. The blood count showed 4,710,000 erythrocytes, 6,100 leukocytes, 53 per cent hemoglobin, 53 per cent polymorphonuclear neutrophils, 44 per cent lymphocytes and 3 per cent eosinophils. The sedimentation rate of the erythrocyes showed marked acceleration, being twenty-two minutes according to the method of Linzenmeyer. The tuberculin test was positive with a dilution of 1 : 10,000 and negative with one of 1 : 100,000. Inoculation of a guinea-pig with material from a lesion on the patient's trunk gave negative results.

A roentgenogram of the lungs revealed moderate interstitial changes and fibrosis of the roots extending throughout both lungs. The apexes were clear. A roentgenogram of the bones did not show any changes.

Histologic examination of a nodular lesion excised from the right shoulder was made by Dr. T. J. Riordan, who reported as follows: "The epidermis is thinned. The basal portion is disrupted by invasion of the infiltration from the corium. A parakeratotic scale covers the rete. The upper third of the corium shows in the midsection a group of moderately infiltrated nodules. A similar large nodular infiltration is noted deep in the corium at one end of the specimen.

Fig. 1 (case 1).—January 1934. Plaques suggesting lupus erythematosus appear at the canthi of the eyes, while nodules are present at the alae nasi, on the vermilion borders of the lips and on the forehead.

The nodules consist of demarcated areas of infiltration merging together or separated by fibrous tissue. Giant cells and epithelioid cells in a flimsy reticulum compose the nodules which can be considered tubercles. The pathologic diagnosis is tuberculosis, probably lupus vulgaris" (fig. 4).

Histologic examination of the keloid-like lesion in the left antecubital region showed at one end of the specimen a great amount of fibrosis and tubercles, composed of typical giant cells, epithelioid cells and round cells. The Ziehl-Neelsen stain did not show any acid-fast bacilli.

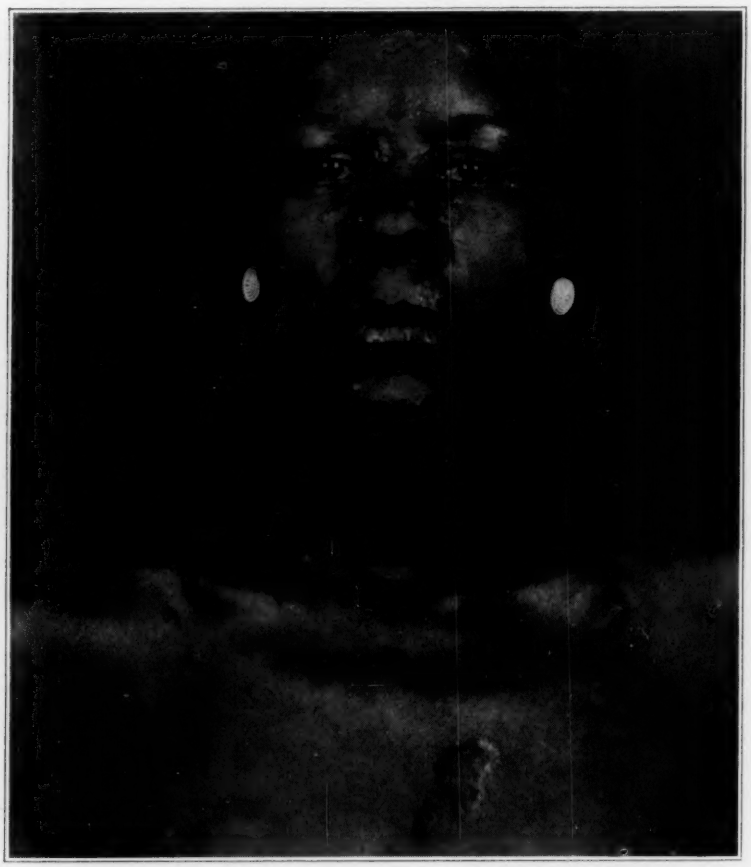

Fig. 2 (case 1).—November 1934. Plaques appear on the trunk, and the eruption on the face has extended. (Compared with that in figure 1.)

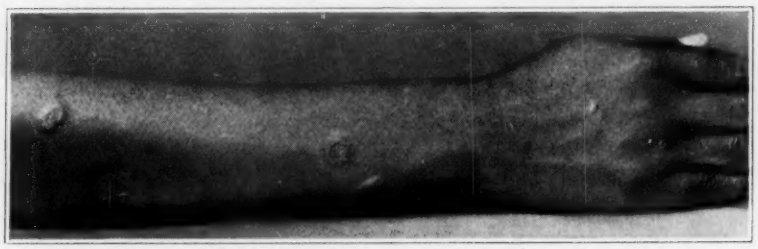

Fig. 3 (case 1).—Round lesions on the extremities.

The pathologic examination of the flat lesion on the right forearm showed the same formation of tubercles as did the keloid-like lesion, and here also no acid-fast bacilli were found.

A diagnosis of tuberculosis cutis associated with latent syphilis was made.

Course and Treatment.—During the first two months the patient was put on a diet poor in salt and high in vitamins and received several injections of neo-

Fig. 4 (case 1).—Section from a nodule on the shoulder, showing tubercles merging or separated by fibrous tissue.

arsphenamine and bismuth subsalicylate. The lesions in the pubic and crural regions improved considerably, but those on the rest of the body were unchanged. During the fourth week of observation the patient began to complain of a productive cough and loss of weight. She was then referred to the Bellevue Hos-

pital, where she was under our observation until Aug. 14, 1934. During her stay in the hospital a few new lesions developed on the extremities, and after a complaint of soreness in the nose it was found that the anterior portion of the septum on the right side and the anterior third of the inferior turbinate on the left side were infiltrated and inflamed. A number of injections of gold sodium thiosulfate did not affect the cutaneous eruption in any way. The patient was under our care in the clinic until the end of November 1934. She did not return for further treatment or observation.

Case 2.—N. F., a Negro aged 29, born in the United States, came to the dermatologic clinic of the Bellevue Hospital on Sept. 18, 1934, presenting a generalized nonpruritic eruption of four years' duration. This started on the legs and gradually spread over the arms, the back of the neck, the trunk and, finally, the face. The patient had been in good general health until two years previous to his first visit to the clinic. At that time he began to feel weak, and he had lost 20 pounds (9.07 Kg.) since then. He gave no history of a cough, pain in the chest, night sweats or hemoptysis. He stated he had no venereal disease.

Cutaneous Eruption.—On the back of the neck there were several irregularly shaped dollar-sized patches of aggregated papules. These patches showed areas of depigmentation, scaling and superficial scarring. Similar patches were present in the left submaxillary region, the left groin and the right side of the abdomen above the anterior iliac spine. Papules varying in size from that of a lentil to that of a pea, with atrophic scars in the center, were scattered over the neck, the upper part of the back, the forehead and the chin. Papules the size of a pinhead and somewhat larger were located on the chin, on the alae nasi and near the inner and outer canthi of both eyes.

On the extensor, and to a lesser degree on the flexor, surfaces of the extremities and on the left wrist, the chest and the scalp there were round and oval plaques, varying in size from that of a lentil to that of a bean, with slightly raised, hyperpigmented borders and depigmented, erythematous, scaly centers. Thus, there were three types of lesions: raised infiltrated patches the size of a half-dollar, with depigmentation and scarring; elevated papules varying in size from that of a pin head to that of a lentil and round and oval flat plaques resembling lupus erythematosus. The mucous membranes were not involved.

General Examination.—The temperature varied between 98 F. in the morning and 101 or 102 F. in the evening. The lymphatic glands in the posterior cervical, postoccipital, anterocervical, supraclavicular, axillary, epitrochlear and inguinal regions were enlarged, firm and devoid of tenderness. The spleen was firm and palpable 2 fingerbreadths below the costal margin. The liver was not palpable. A roentgenogram of the spleen did not reveal any abnormality. Auscultation of the heart revealed a long, soft, high-pitched systolic murmur over the sternum, above the second intercostal space in the right upper quadrant of the chest and in the supraclavicular region. Percussion of the right lung revealed dulness posteriorly from the tip of the scapula to the level of the sixth thoracic vertebra. Medium and fine râles were heard anteriorly and posteriorly over the entire lung.

A roentgenogram of the lungs showed dense fibrosis and calcification of the roots, patches of consolidation at the lower lobe of the right lung, just above the diaphragm, mottling throughout the entire right lung and the lower half of the left lung, a suspicious cavitation in the upper lobe of the right lung, interstitial fibrotic changes in the region adjacent to the cardiac outlines and obliteration of the costophrenic sinus by adhesions. A roentgenogram of the bones did not reveal any pathologic changes. The sputum was negative for tubercle bacilli.

In the department for tuberculous patients of the Bellevue Hospital, where the patient was under observation for some time, his condition was diagnosed as advanced pulmonary tuberculosis with marked fibrosis.

Histologic examination of an axillary node revealed a normal fibrous capsule and numerous tubercles separated from each other by small strands of lymphocytes. Many tubercles contained giant cells of the Langerhans type, but there was no caseous necrosis. The pathologic diagnosis was tuberculosis.

Histologic examination of the flat lesion of the arm and the nodule of the neck showed the same pathologic picture of tuberculosis cutis (fig. 5). No acid-fast bacilli could be detected.

The blood count showed 5,700,000 erythrocytes, 5,800 leukocytes and 82 per cent hemoglobin. The differential count showed 66 per cent polymorphonuclear neutrophils, 22 per cent lymphocytes, 6 per cent mononuclears and 2 per cent eosinophils.

The tuberculin test was negative with a 1:10,000 dilution but positive with a dilution of 1:1,000. The Wassermann test of the blood was negative.

The patient was discharged from the hospital's department for tuberculous patients as improved in general condition on Oct. 31, 1934. He has not returned for observation or treatment of his cutaneous eruption.

DIAGNOSIS OF THE CUTANEOUS ERUPTION

The only absolute proof of tuberculosis of the skin lies in the finding of tubercle bacilli in the lesions and the positive results of inoculation of guinea-pigs. No tubercle bacilli were found in the lesions in either patient, and inoculation, carried out only in the first case, gave negative results. In spite of these negative findings, the diagnosis of tuberculosis cutis can be maintained with reasonable certainty from the combination of the following factors: the tuberculous histologic structure, the marked pulmonary changes, particularly in case 2, the markedly enlarged lymphatic glands, which were examined microscopically in case 2 and found to have a tuberculous structure, and the history. The history revealed in the first case the constant association of the patient with a brother who had died of pulmonary tuberculosis, and in the second case a progressive loss of weight. The diagnosis will be corroborated later by similar cases reported in the literature, in which the diagnosis of tuberculosis was proved.

That eruptions like these do not fit into any of the previously known clinical entities can be surmised easily from the discussion which these two cases elicited when they were presented by Fox and Maloney [5] before the Atlantic Dermatologic Conference. Weidman put the eruption into the group of ulcerative sarcoid. Klauder expressed the opinion that it belongs in a group of conditions which during the early period of their course resemble sarcoid of Boeck but later assume features which distinguish them from sarcoid and other clinical types of tuber-

5. Fox, H., and Maloney, E. R.: Tuberculosis Cutis, Arch. Dermat. & Syph. **32**:945 (Dec.) 1935.

culosis. These features are frequent involvement of the scalp, a psoriasiform character of the lesions, ulceration and a tendency of the lesions to follow the lines of cleavage. According to Klauder, the histologic

Fig. 5 (case 2).—Section from a papule on the back of the neck, showing tubercles.

picture is unlike that of sarcoid and more like that of "bacillary tuberculosis," as it commonly affects the viscera. Sulzberger stated that he had never encountered this type of tuberculosis in white persons in Europe, and that the eruption seemed to him a combination of sarcoid,

hematogenous lupus vulgaris and lupus miliaris disseminatus. Ketron also considered it a clinical variety which one could not classify with other well known types of tuberculosis.

When the first patient was presented by Fox [6] before the Manhattan Dermatologic Society Rosen remarked that the diagnosis of generalized lupus vulgaris needed further corroboration by inoculation of animals. Andrews had the impression that the condition was disseminated lupus erythematosus. MacKee diagnosed it as cutaneous tuberculosis, probably lupus vulgaris, with formation of an unusual amount of connective tissue, and Wise agreed with the diagnosis of generalized lupus vulgaris.

These diverse opinions of experienced dermatologists testify to the unusual picture of the eruption and particularly to the great difficulty in exact classification, although there is agreement among most of the discussers as to the tuberculous nature of the eruption and its status as a special clinical variety.

The reports of similar cases in the literature and the opinions of authors and discussers of these cases will give a better insight into, and understanding of, the type of eruption with which we are dealing in this paper.

REVIEW OF SIMILAR CASES IN THE LITERATURE

One of the most important cases was reported by Klauder [7] in 1925 under the title "Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature." The patient was a Negress whose eruption was identical with those shown in our cases. In addition to enlargement of the lymph glands and inactive pulmonary tuberculosis, she showed changes of an undetermined nature in the phalanges. After twenty-one months the lesions underwent involution with scarring and with or without preceding ulceration. The scars were soft and pliable, as in syphilis. Because of the sarcoid-like lesions on the face, the brownish nodular lesions elsewhere, the evolution and the histologic picture Klauder considered the diagnosis of cutaneous tuberculosis. However, in his opinion, the eruption conformed better to the conception of tuberculid than to that of "bacillary tuberculosis," because of the extensive, disseminated and symmetrical distribution of the eruption, the tendency to spontaneous cure and, perhaps, the negative reaction of animals to inoculation. He expressed the belief that "tuberculosis was suspected but not proved." However, one year later Klauder and Weidman [8]

6. Fox, Howard: Generalized Lupus Vulgaris in a Syphilitic Patient, Arch. Dermat. & Syph. **30**:321 (Aug.) 1934.

7. Klauder, Joseph V.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, Arch. Dermat. & Syph. **12**:171 (Aug.) 1925.

8. Klauder, Joseph V., and Weidman, Fred D.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, Arch. Dermat. & Syph. **13**:675 (May) 1926.

reported that shortly before the death of the patient tubercle bacilli were found in the sputum and that the necropsy revealed an extensive tuberculous ulcerative enteritis with massive caseous tuberculosis in the lungs. The latter observation is of interest, for one year prior to the patient's death a roentgenogram failed to show any marked changes in her lungs.

This case is of importance, for in spite of the abundance of tubercle bacilli in the visecra no tubercle bacilli could be obtained from the cutaneous lesions. According to Klauder and Weidman the case was "in all probability a unique and a hitherto undescribed instance of what conforms to our present conception of a tuberculide."

In 1929 Traub [9] presented before the New York Dermatological Society a 36 year old Negress with a generalized eruption of seven years' duration which resembled the previously described type. The second and third fingers were spindle-shaped and in the roentgenogram showed absorption and shortening of the digits. The histologic examination revealed "typical tuberculosis cutis." In the discussion MacKee called attention to the grouped small nodules around the alae nasi and mouth and on the forehead which "look like lesions of lupus miliaris and occur only in the colored race."

In the same year Gage [10] presented a like case with the diagnosis "tuberculosis cutis or sarcoid." The tuberculin test was negative, and the microscopic examination showed typical tuberculous structure resembling that of the "usual varieties of tuberculosis." Weidman diagnosed the condition as miliary lupoid of Boeck. At the same meeting Ginsburg [11] presented a similar case with the diagnosis "tuberculosis cutis," which diagnosis was accepted.

In 1931 Rauschkolb [12] presented two similar cases with the diagnosis "tuberculosis cutis." Both patients showed involvement of the palpebral conjunctivae and of the oral mucous membranes. Besides the usual type of lesions, there were subcutaneous nodules. The tuberculin test was positive in one case with a dilution of 1 : 1,000 and in the other with a dilution of 1 : 10,000.

In the discussion Ormsby remarked that "such cases should be classified as types of cutaneous tuberculosis without trying to put them in any particular pigeonhole."

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9. Traub, Eugene F.: Tuberculosis Cutis, Arch. Dermat. & Syph. **19**:137 (Jan.) 1929.

10. Gage, A. J.: Tuberculosis Cutis or Sarcoid, Arch. Dermat. & Syph. **19**: 996 (June) 1929.

11. Ginsburg: Tuberculosis Cutis, Arch. Dermat. & Syph. **19**:995 (June) 1929.

12. Rauschkolb, J. E.: Tuberculosis of the Skin, Arch. Dermat. & Syph. **23**:155 (Jan.) 1931.

In the case presented by Shaw [13] in 1931 there was a positive Wassermann test. Wile diagnosed the condition as disseminated tuberculosis of the skin and not a tuberculid or lupus vulgaris. Michelson called it nodular sarcoid and Finnerud considered it a tuberculid that was "closely related to sarcoid but was not definitely sarcoid."

In 1933 Crawford [14] reported, under the title "Nodulodiscoid Tuberculosis of Anergic Type with Development into Active [allergic] Pulmonary Tuberculosis," two such cases. In one, there was enlargement of the liver and spleen, and the patient later died of pulmonary tuberculosis. In the other, acid-fast granules and coccoid forms were noted in cultures of material from the inguinal glands, and the subcultures showed variously shaped fungoid forms which were considered phases in the mutation of tubercle bacilli.

In the case presented by Cannon,[15] some of the lesions were ulcerated, and a few were rupial. Microscopic examination of a lesion from the lip showed tubercles with necrosis in the center. Sulzberger remarked that the lesions on the body looked like sarcoid of Boeck and those on the face like lupus miliaris faciei. Wise expressed the thought that the patient had a combination of various tuberculous changes in the skin and that such an eruption is seldom encountered in white persons.

Under the title "Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes" Nomland [16] in 1934 reported six cases, several of which resembled closely those reported in this paper.

In 1935 Machacek [17] presented such a case in a 27 year old Negro who had also subcutaneous nodules and lesions on the palms. Histologic examination showed typical tubercles. A roentgenogram of the skull showed numerous irregular and rounded shadows of increased density between the tables.

Senear and Schorr [18] presented a 22 year old Negro with a generalized papulonodular eruption. The histologic picture of a subcutaneous nodule showed tuberculous structure with central caseation and necrosis. In the discussion Nomland suggested the name "hematogenous cutaneous

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13. Shaw, Henry C.: A Case for Diagnosis (Tuberculosis of Skin? Sarcoid?), Arch. Dermat. & Syph. **23**:1159 (June) 1931.

14. Crawford, Stanley: Cutaneous Nodulodiscoid Tuberculosis of Anergic Type with Development into Active Pulmonary Tuberculosis, Arch. Dermat. & Syph. **27**:766 (May) 1933.

15. Cannon, A. Benson: A Case for Diagnosis (Tuberculosis of the Skin?), Arch. Dermat. & Syph. **29**:755 (May) 1934.

16. Nomland, Ruben: Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes, Arch. Dermat. & Syph. **30**:59 (July) 1934.

17. Machacek, G. F.: Tuberculosis of the Skin, Arch. Dermat. & Syph. **31**:114 (Jan.) 1935.

18. Senear, F. E., and Schorr, Henry C.: Cutaneous Tuberculosis, Arch. Dermat. & Syph. **32**:169 (July) 1935.

tuberculosis." Senear expressed the belief that clinically such eruptions resembled sarcoid, although the histologic structure was not that of sarcoid but that of tuberculosis.

In 1935 Klauder [19] presented an 18 year old Negress the eruption on whose skin was associated with opacities on the cornea. The discussers made the diagnosis of tuberculosis cutis and put the eruption into the group described in the foregoing paragraphs.

Greenbaum [20] in 1936 presented a 22 year old Negress who had a generalized papular eruption, the lesions of which were mostly annular, some being capped with crusts and others covered with silvery scales. His diagnosis was "cutaneous tuberculosis (sarcoid type)." The patient had become blind because of tuberculous keratitis. Inoculation of a guinea-pig with macerated material from a lymph node gave positive results, although no organisms were obtained by smear. The reaction to a tuberculin test was negative. A roentgenogram of the lungs showed probable tuberculous infection of the hilar region, with miliary distribution throughout the lungs. On examination with the cystoscope numerous tubercles were seen in the region of the right ureteral orifice and on the right lateral wall of the bladder.

In the discussion Stokes remarked that "the association of certain types of extensive cutaneous tuberculosis with comparatively good health is one of the interesting and paradoxic features of tuberculosis in the Negroes."

ANALYSIS OF THE CASES REPORTED IN THE LITERATURE

The eruption repeatedly described in the cases heretofore enumerated is identical with the eruption in our two cases and has the following features: It is widespread and often generalized. It involves different areas of the face, particularly the vermilion borders of the lips, the alae nasi, the eyelids, the canthi of the eyes, the ears, the neck, the trunk, the buttocks and the extremities. In some cases there is also involvement of the conjunctivae and the mucous membranes of the mouth. The scalp, the palms and the soles are less frequently involved. The condition usually begins with a few papules or nodules on some part of the skin and gradually extends to other parts over a period of months or years.

The eruption is multiform, consisting of round or ovoid, flattened or elevated papules from 1 to 10 mm. in diameter. Those on the vermilion borders of the lips and on the nostrils are discrete and usually translucent; some show a yellowish spot which suggests

19. Klauder, Joseph V.: A Case for Diagnosis, Arch. Dermat. & Syph. **31**:250 (Feb.) 1935.

20. Greenbaum, S. S.: Cutaneous Tuberculosis (Sarcoid Type), Arch. Dermat. & Syph. **33**:751 (April) 1936.

necrosis. Those on the body are frequently arranged in linear formation or in plaques. Other lesions are intracutaneous or subcutaneous nodules, granulomatous infiltrations or psoriasiform plaques from 2 to 10 cm. in diameter. Not infrequently linear keloid-like raised lesions are seen, especially on the neck, on the shoulders and in the antecubital regions. These result from fibrosis of the primary lesions, due to the tendency of the skin of Negroes to the formation of keloids. Some of the lesions undergo superficial ulceration and then, after a variable period of time, undergo involution and disappear, leaving soft depigmented scars resembling those of syphilis. Others may heal without preceding ulceration but leave similar scars.

The duration of the eruption varies between six months and seven years, and it takes several months or years for an eruption to develop. There are no subjective symptoms except slight pruritus at times. In most cases there are enlarged lymph glands, which are firm and painless and do not break down. On histologic examination tuberculous structure is found. In one case inoculation of a guinea-pig with material from a lymph gland gave positive indications of tuberculosis.

The lungs are involved in the majority of the cases, the degree of involvement varying from slight changes to marked infiltration and cavitation. In most of the cases the condition was considered quiescent or arrested. Tubercle bacilli were found in the sputum of one patient shortly before death. In another case acid-fast granules were seen on histologic examination of an inguinal gland and in material from that gland coccoid forms were demonstrated on culture.

The tuberculin test was positive in most of the cases in a dilution of 1 : 1,000. One patient whose reaction has been negative to tuberculin gave a positive reaction when pulmonary and visceral tuberculosis developed.

In some cases there were changes in the phalanges or in the bones of the skull. In one case there was tuberculous involvement of the intestines and the mesenteric lymph glands. In another the genitourinary tract was involved. In some cases there was enlargement of the liver and the spleen.

The histologic structure of the cutaneous lesions was tuberculous in most of the cases, though occasionally a tuberculoid structure was found. Some lesions showed central necrosis.

The ages of the patients varied between 22 and 43 years, the majority being in the third decade. More women than men were affected.

COMMENT

There is no doubt that the foregoing repeatedly described eruption is a form of tuberculosis cutis. The question which frequently comes up in discussions relates to the exact classification. We agree with

Nomland and others who consider it best to call this type of eruption "hematogenous tuberculosis of the skin in the Negro." The clinical picture, the histologic observations and the positive allergic response to tuberculin speak against sarcoid. If one were forced to give a more specific name, tuberculosis indurativa would suggest itself, as most of the lesions would fit into the group designated by that name. Michelson and Winer [21] expressed an opinion similar to ours. They stated that "until these cases of more or less widely disseminated papular forms of tuberculosis in Negroes are carefully studied and evaluated it is best not to arrive at a definite decision as to classification." The usual polymorphism of the eruption, the general distribution and the course, which are unlike those in any of the forms of tuberculoderma encountered in the white race, impress us as a clinical entity of cutaneous tuberculosis peculiar to the colored race.

CUTANEOUS TUBERCULOSIS AND SYPHILIS

The appearance of the eruption in case 1 during antisyphilitic treatment raises the question of the rôle of syphilis in the manifestation of cutaneous tuberculosis. Stokes [22] remarked that "the well recognized possibility that syphilis superimposed on a latent tuberculosis may cause a flare-up of the latter must always be borne in mind." He [23] mentioned having seen "only once a definite example of what he thought might be a lighting up of a tuberculous process by treatment for syphilis."

Lelong, Marcel and Rivallier [24] expressed the belief that syphilis is "anergizing," like measles, varicella, etc., for they found decreasing reactivity to tuberculin parallel with the generalization of the syphilitic infection, the lowest reactivity occurring in florid secondary syphilis.

Ritter [25] observed reactivation of cervical tuberculous lymphadenitis in syphilitic sclerosis of the lip.

In the case described by Shaw [13] the tuberculous eruption appeared in a Negro who had a strongly positive Wassermann reaction. After antisyphilitic treatment the patient acquired an exfoliative dermatitis, while the orignal eruption disappeared. The eruption reappeared following exfoliation.

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21. Michelson, H. E., and Winer, L. H.: Tuberculodermas of the Face, Arch. Dermat. & Syph. **29**:251 (Feb.) 1934.

22. Stokes, John H.: Modern Clinical Syphilology: Diagnosis, Treatment, Case Studies, Philadelphia, W. B. Saunders Company, 1926, p. 512.

23. Stokes,[22] p. 380.

24. LeLong, Marcel, and Rivallier, E.: Syphilis et tuberculose: L'anergie syphilitique, Compt. rend. Soc. de biol. **88**:327, 1923.

25. Ritter: Ueber den Zusammenhang von Lues und Tuberkulose, Dermat. Wchnschr. **79**:1587, 1924.

Busman [26] presented a Negress with a generalized tuberculous eruption of the skin of one year's duration, who also had a strongly positive Wassermann reaction of the blood. Antisyphilitic treatment reversed the serologic reaction, but the eruption persisted.

Beck [27] reported three cases of simultaneous development of tuberculosis and syphilis. He expressed the belief that "there is some evidence that syphilis predisposes to tuberculosis."

Alfredo Mario,[28] after an investigation of 120 cases of syphilis associated with pulmonary tuberculosis, concluded that syphilis does not predispose the patient to tuberculous infection, that recently acquired syphilis may aggravate existing tuberculosis and that syphilis of long standing has no influence on the evolution of tuberculosis. He expressed the belief that antisyphilitic therapy does not affect, favorably or unfavorable, the course of a tuberculous infection of the lungs.

Bloom [29] presented a white woman in whom during treatment for a recently acquired syphilitic infection a generalized papular eruption developed, which on histologic examination showed typical tubercles.

In one of the cases reported by Nomland [16] the tuberculous eruption appeared on the face of the patient during antisyphilitic therapy and improved under treatment with tuberculin.

We feel that in our patient the syphilitic infection might have contributed in some way to the manifestation of the cutaneous tuberculous eruption.

SUMMARY

Two cases of generalized tuberculous eruption in Negroes are reported. A review is made of numerous similar cases reported in the literature or presented before dermatologic societies. An attempt has been made to show that we are dealing with a hematogenous tuberculous eruption peculiar to the Negro which deserves to be considered a clinical entity. In one of the reported cases the eruption appeared while the patient was receiving antisyphilitic treatment. We believe that the syphilitic infection was a factor in the appearance of the tuberculous eruption of the skin in this patient.

135 East Fiftieth Street.

175 West Seventy-Ninth Street.

26. Busman, G. J.: Disseminate Miliary Tuberculosis, Arch. Dermat. & Syph. **26**:194 (July) 1932.

27. Beck, J.: Gleichzeitiges Vorkommen von Tuberkulose und Lues, Ztschr. f. Laryng., Rhin., Otol. **24**:472, 1933.

28. Mario, Alfredo: Syphilis and Tuberculosis, Rev. méd. latino-am. **19**:240 (Dec.) 1933.

29. Bloom, David: Lupus Miliaris in a Syphilitic Patient, Arch. Dermat. & Syph. **25**:566 (March) 1932.

LESIONS OF THE SKIN AND SUBCUTANEOUS TISSUE IN DISEASES OF THE PERIPHERAL CIRCULATION

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It is evident that continued circulatory deficiency must produce changes in the nutrition of the affected area. The essential change is the development of fibrosis. On clinical grounds these complications of circulatory deficiency may be divided into two groups. In one group, which may be called the "chilblain" group, the lesions are subacute and localized and individually tend to clear up, while in a second group there is a slow persistent and relentless interstitial fibrosis such as is seen in acrosclerosis.

While in the first group it is evident that a defective venous return is the cause, the lesions in the second group appear to arise from an insufficient arterial supply.

GROUP I

The feature of the first group is the formation of subcutaneous nodules, which commonly disappear in time but occasionally break down and lead to a painful and tedious ulceration. The study of these nodules is best begun by observing them as they occur in cases of old anterior poliomyelitis.[1]

Anterior Poliomyelitis.—The child who at the age of 2 or 3 years suffers from severe acute anterior poliomyelitis is left with extensive motor paralysis but does not for some years suffer from circulatory troubles. It is often about the age of from 10 to 12 years that these begin. On the leg, which is usually cyanotic and cold, there begin to develop small subcutaneous nodules. These are from 1 to 2 cm. in diameter, firm, painful and tender, and are situated just below the skin and adherent to it. They are reddish purple. Some patients say they know when these lumps are coming because their appearance is preceded by a period of troublesome itching. The usual site is the lower half of the posterior aspect of the leg. At first these

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Lecture delivered for the University of London at St. Mary's Hospital Medical School, Feb. 16, 1937.

1. Telford, E. D., and Stopford, J. S. B.: Brit. M. J. **2**:770 (Oct. 28) 1933.

nodules appear only in winter; they last for several weeks and disappear with the advent of warmer conditions. After a few years the nodules may appear in the summer also, and some of those which appeared in the previous winter may fail to resolve and may ulcerate. They form small clearcut ulcers with a tenacious fawn-colored slough in their floor and are tedious in healing, often lasting well into summer before closing. They become more frequent and severe as time goes on and may finally leave one or more large chronic ulcers which completely fail to heal.

These conditions are more commonly seen in patients belonging to the poorer classes, who have little chance of obtaining the warmth and care which the limbs need.

The nodules and ulcers are clearly related to defective circulation, and in considering their etiology the following factors come up for consideration: defective venous return, a relatively small arterial inflow, a great excess of fat and the effect of local cold. All these factors appear to play a definite part in causing the condition.

The deep purple cyanosis—Krogh's subcutaneous lake of ink—shows the extent of the defective venous return. The explanation lies no doubt largely in the loss of muscle. In the normal limb blood is propelled along the numerous and large veins draining muscle by contractions of the muscle itself, and this action depends on the valves within the veins. In the limb injured by anterior poliomyelitis such a mechanism is lost. That this is the important factor is, I think, proved by the fact that in limbs which have retained a fair amount of voluntary muscle power cyanosis is slight and nodules and ulcers do not occur. I think that some part is played also by the tough fascial stocking of a normal limb. If this stocking is incised, as when a fascial graft or a Kondoleon operation is performed, the underlying muscle belly herniates at once into the incision, showing that the fascia is normally exerting pressure. This pressure must be experienced by the intermuscular veins, and if such pressure is abolished—as it is in the limb injured by anterior poliomyelitis—the veins dilate and the current is slowed.

The decrease in arterial inflow can be proved in striking fashion when the abdomen of a patient with this condition is opened for a lumbar ganglionectomy. In older children and in adults who have suffered from severe anterior poliomyelitis since early childhood the external iliac artery is found to be much reduced in size; I have often found it to be no larger than a radial artery. The artery, having no longer to meet the demands of increasing muscular activity in a growing limb, has ceased to develop normally. This means that a smaller supply of blood is entering a limb already suffering from a

defective return mechanism. That this is so is shown by the results of experiments on baking these limbs in an electrically heated cradle. It is easy to find a child in whom one leg is grossly damaged by anterior poliomyelitis while the other leg is normal or but slightly affected. If both limbs are baked for twenty minutes at 50 C. the damaged leg becomes heated much more quickly than the sound one; its defective circulation is carrying off much less heat. If the limbs are removed from the cradle and allowed to cool, the damaged limb cools much more slowly than the sound one, again because its defective circulation is removing less heat and because much less cool blood is entering it from the body than is the case with the sound limb.

It is a common observation that the limb, although severely paralyzed, does not differ greatly in girth from its sound fellow. The girth of the involved limb is due entirely to fat, as can be shown by picking up the subcutaneous tissue between the fingers and the thumb. The difference between a paralyzed and a sound limb in this respect is obvious. Still more obvious is the enormous deposit of fat seen if a cross-section is taken through a paralyzed leg. It will be seen that with the exception of the bones and a trivial amount of wasted muscle nearly the whole limb is composed of fat. Fat is a poorly nourished material susceptible to injury and to cold. This explains why these nodules and ulcers occur over the calf, where the fat is deepest.

I turn now to a condition which is clearly closely allied to the vascular lesions of anterior poliomyelitis, i. e., erythrocyanosis.

Erythrocyanosis.—The condition is a reddish blue discoloration of the skin seen on the lower half of the legs in girls and young women; it is especially evident in the region above the malleoli. In this respect it differs from acrocyanosis, acro-asphyxia, which affects the areas served by most peripheral parts of the circulation, i. e., the digits, the ears and the nose. Erythrocyanosis may affect the skin over the triceps muscle in the arm but seldom leads to any serious consequences in this situation. Examples of the disease in males are rare.

General Features: In its minor degrees the lesion in the legs is common and trivial, but it may develop in some cases into a serious and even crippling disability. In advanced stages the following features are present: The lower half of the leg, particularly in its posterior surface, is of a purplish hue, which may be uniform or marked by scattered plaques of a deeper color. The color is blanched by pressure, and the discolored area is cold to the touch. The circumference of the limb is much increased by a firm, elastic infiltration of the subcutaneous tissue. This may reach considerable dimensions and may take the form of a thick and prominent cuff of tissue most evident just above the malleoli and decreasing higher up on the leg. It produces a clumsy and

evident deformity. The overlying skin is characteristic; it is stippled with small reddish points in the center of which is a minute keratinized focus. These are the hair follicles, enlarged and pigmented; the hair is usually absent—the *keratose pilaire* described by French authors.

From time to time fairly large and distinct indurated nodules appear in the subcutaneous tissue. When fully developed, those nodules form circular plaques from 1 to 2 cm. in diameter. On inspection the overlying skin appears a little tense and reddened, and on palpation a definite discrete induration is found, which spreads deeply into the subcutaneous tissue. These nodules undergo a slow resolution which at best occupies several weeks. They often leave evidence of subcutaneous scarring, and in one of our patients, a middle-aged woman who had suffered for many years, there was a large area of thin fibrous skin on the lower half of the posterior aspect of each leg. The patient definitely stated that at no time had there been any ulceration. On the other hand, in a number of cases a nodule here and there enlarges, becomes acutely inflamed and finally bursts, leaving a small circular ulcer in the base of which is a tough adherent slough. These ulcers are slow to heal and often last until the beginning of summer. In the cases of more severe involvement sensation of weight and coldness in the leg, intolerable itching and burning pain, together with the appearance of ulcers, may render the patient quite unfit for work.

The thin, spare leg appears almost immune to this disease. Persons suffering from the condition are of a stout and florid build with large limbs, the sturdy appearance of which is misleading and due to excessive fat. Their general appearance is that of rude health, and Mach,[2] who gave a good description of the lesion, stated that the patients excite no pity because they look so healthy.

The resemblance between the nodules in this disease and the nodules of anterior poliomyelitis is at once apparent. They occur in the same positions on a fat and cyanotic leg when the limb is exposed to cold, and they run exactly the same clinical course. A study of erythrocyanosis must lead at once to the condition known as Bazin's disease.

Bazin's Disease.—As the result of numerous clinical observations I am of the opinion that Bazin's disease is not tuberculous and is in no way different from erythrocyanosis. Bazin's[3] original description in 1861 would stand for a description of erythrocyanosis. He described the nodules, mentioned their predilection for the lower part of the leg and stated that the condition occurs in fresh-complexioned and stout

2. Mach, R. S.: Rev. méd. de la Suisse Rom. **49**:804 (Nov. 25) 1929.

3. Bazin, A. P. E.: Leçons théoriques et cliniques sur la scrofule, ed. 2, Paris, A. Delahaye, 1861.

young women. He said, "I have often met with it in the legs of young washerwomen," an observation which points to the effect of cold on the bare legs as a cause.

There is, I submit, no evidence of the tuberculous nature of Bazin's disease. In four cases referred to me by dermatologists with the diagnosis of Bazin's disease, I have excised nodules for examination. Sections from these nodules showed no evidence of tuberculosis although they were specially examined and stained for the purpose; material from them produced no evidence of tuberculosis when inoculated into guinea-pigs. In this respect I confirm the observations of Audry.[4] It is likely that the main source of confusion is the presence of giant cells in the nodules. It is probable that by some authors these cells have been regarded as evidence of tuberculosis. They are, however, giant cells of "foreign body type," and on close examination and special staining they do not show tubercle bacilli. Some dermatologists point to old scars in the neck or to a positive Mantoux reaction as evidence that Bazin's disease is tuberculous, but in view of the frequent occurrence of these manifestations in all sorts and conditions of men such arguments are of little weight.

To explain the fact that bacilli are not observed in the nodules some writers fall back on a theory of tuberculous virus. A theory like this, resting as it does on a nebulous and speculative basis, is difficult to combat, but it may be pointed out that the same theory in the form of the *rheumatisme tuberculeux* of Poncet has never received any wide acceptance among surgeons best qualified to judge.

Finally, I find it difficult to visualize a tuberculous lesion which can appear in winter and clear up in summer.

The question is not merely an academic one, it has a practical side. Hundreds of patients with this condition are subjected to the social and occupational stigma of attending tuberculosis clinics for treatment of a condition the tuberculous nature of which is, to say the least, highly doubtful.

Histologic Picture of the Nodules.—The nodules of erythrocyanosis, of anterior poliomyelitis and of Bazin's disease show histologic pictures which are identical. In each the outstanding features are as follows:

1. A thickening of the smaller arterioles, all three coats being affected, and a dense perivascular lymphocytic infiltration (figs. 1 and 2).

2. The presence in some cases of numerous giant cells swollen by fat (figs. 3 and 4).

3. Fat necrosis in various stages of resorption. This is the dominant picture (figs. 5 and 6).

4. Audry, C.: Ann. de dermat. et syph. **9**:209, 1928.

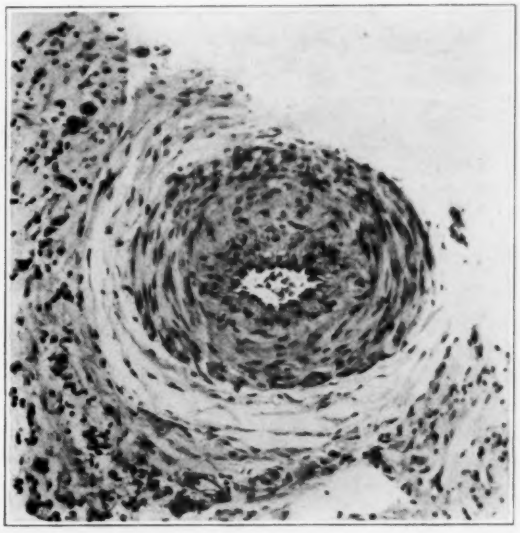

Fig. 1.—Photomicrograph showing thickening of all the coats of the small artery; × 150.

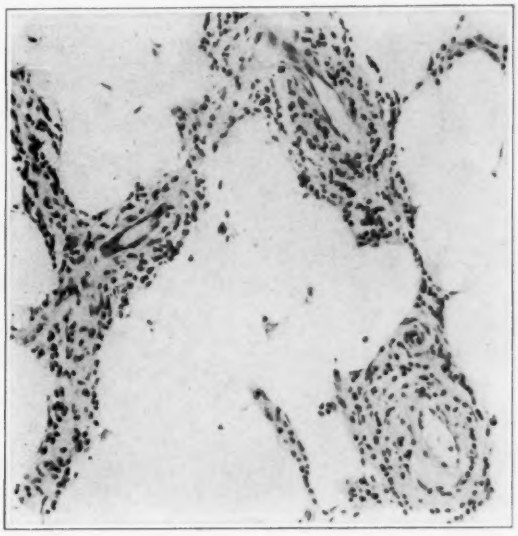

Fig. 2.—Photomicrograph showing lymphocytic infiltration between the fat cells; × 150.

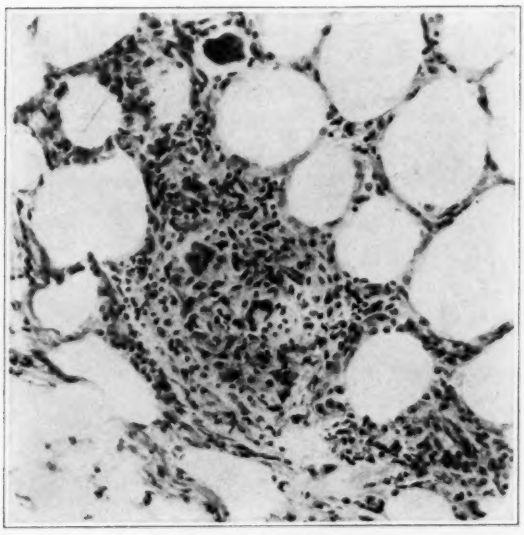

Fig. 3.—Photomicrograph showing a giant cell of foreign body type infiltrated with altered fat; × 150.

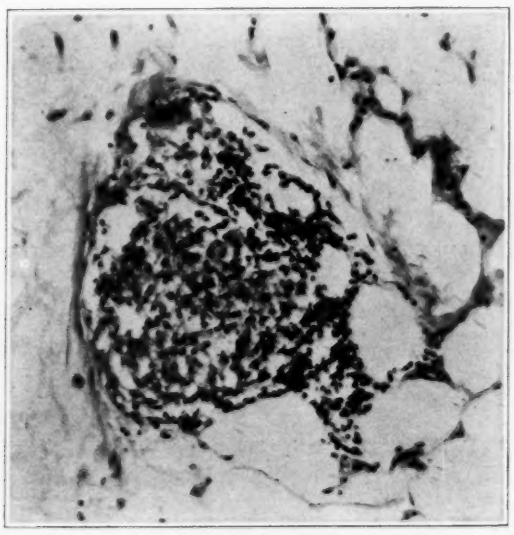

Fig. 4.—Photomicrograph showing a pseudotubercle with reticulated center filled with altered fat; × 150.

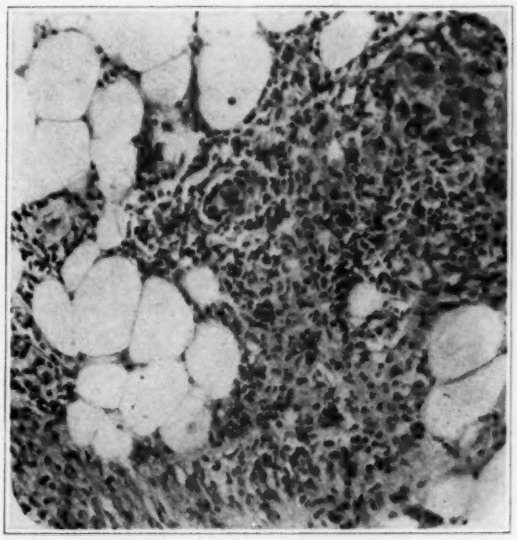

Fig. 5.—Photomicrograph showing young connective tissue with giant cells. The fat cells are altered and are breaking up; × 150.

Fig. 6.—Photomicrograph showing an area of altered fat surrounded by granulation tissue; × 50.

4. The formation of fibroblasts and granulation tissue in the later stages (fig. 7). This is evident at the periphery of the necrosed area.

If sections from the nodules are compared with sections of necrotic fat from the breast an exactly similar picture is seen. In fact, so complete is the identity that unlabeled sections of tissue affected by erythrocyanosis, Bazin's disease, anterior poliomyelitis and fat necrosis of the breast cannot be sorted into their respective groups.

It is well to avoid placing too much reliance on identity of histopathologic pictures. Tissues are subject to a great variety of insults, but their modes of response are limited to a much smaller group of defensive methods. When, however, not merely the histologic pictures

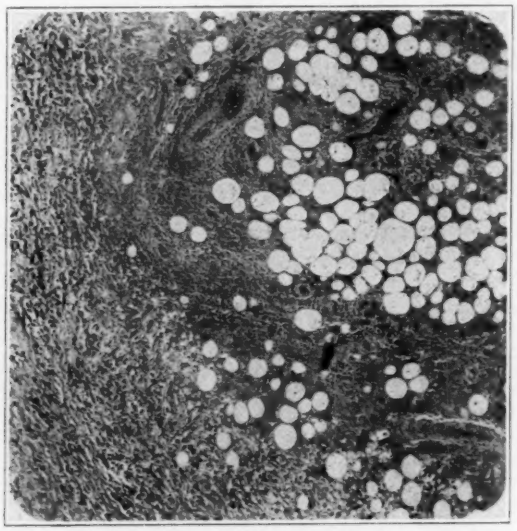

Fig. 7.—Photomicrograph showing a later stage of the process seen in figure 6. There is a beginning of young fibrous tissue; × 50.

but the clinical courses and the appearances agree, one is on safer ground in concluding that the four lesions under consideration are due to a common cause. What that cause is is not known. The picture is one of fat necrosis in consequence of some deleterious agent; this damage is followed by repair. The agent may be some substance which escapes from the blood. The presence of a fat-splitting ferment in blood has long been known.

Hadfield [5] in writing of fat necrosis of the breast stated that the central feature of the process is a slow aseptic saponification of neutral fat by blood and tissue lipase analogous to pancreatic fat necrosis but

5. Hadfield, G.: Brit. J. Surg. **17**:673, 1930.

much milder in degree. Farr,[6] who had studied the subject fully by producing necrosis of subcutaneous fat in pigs, concluded that "possibly no ferment action is concerned, the etiological factor being simply ischaemia." Bartsch [7] in an important article pointed out that fat necrosis is by no means confined to the subcutaneous fat of the breast but occurs in other situations. He described the nodular lesion under the expressive and descriptive title of lipophagous granuloma. Abrikossoff [8] stated: "In the event of various toxic influences or disturbances of circulation in consequence of alteration in vessel walls and vasomotor disturbances a patchy necrosis of fatty tissue can arise. . . . As a result the appearance of free and saponified fat plays the part of a foreign body in the tissue and causes a reaction with the appearance of foreign body giant cells which resorb the fat."

Results of Lumbar Sympathectomy.—The resemblance between the nodules of anterior poliomyelitis, erythrocyanosis and Bazin's disease is further confirmed by the reactions of tissue affected with these respective conditions to removal of the lumbar portion of the sympathetic cord. In cases of severe and crippling persistent ulceration of nodules of anterior poliomyelitis, I have during the past six years operated on sixteen patients. Of these fourteen remain cured, but two have shown some relapse. Similarly, in cases of the chronic ulcerative types of the erythrocyanosis-Bazin group, I have operated on nineteen patients during the six years. Of these, seventeen remained well and two suffered relapses.

GROUP II

The second group of phenomena which may ensue in cases of persistent circulatory disturbance in the extremities is marked by steadily increasing fibrosis. In this group the cause is deficient arterial supply. The results are usually described by the dermatologist as a variety or subclass of scleroderma, as acrosclerosis or as sclerodactylia. It should, however, be pointed out that the lesions involve far more than the skin. They extend into the deeper tissues, involving tendons and their sheaths, causing osteoporosis of phalanges and heavy deposits of calcium (hypodermolithiasis).

The skin of the fingers is at first thickened, losing its suppleness and feeling leathery; later it becomes thin and glossy from tension. Still later small ulcers form over the end of the pulp or over the prominent bones, especially on the little finger. These ulcers are painful and persist for long periods. The nails are small, misshapen and rigid and curve over the tapered ends of the fingers. The fingers themselves

6. Farr, C. E.: Ann. Surg. **77**:513, 1923.
7. Bartsch, G. H.: Arch. f. klin. Chir. **178**:62, 1933.
8. Abrikossoff, A.: Centralbl. f. allg. Path. u. path. Anat. **38**:542, 1926.

become progressively contracted in flexion and produce a fixed clawlike hand. If roentgenograms of hands thus affected are made in all cases, it is seen that some show considerable osteoporosis of bone, especially in the terminal phalanges, and a striking observation in some is the occurrence of considerable deposits of lime salts, usually in the pulp of the digits.

Fibrotic changes of similar type occur in the face, especially in the circumoral region. They consist at first in the formation of deep ridges radiating from the mouth. Later the fibrosis causes much restriction in the opening of the mouth.

These changes develop slowly over a number of years and are preceded by a long period during which asphyxial and cyanotic attacks in the fingers are a prominent feature. Some writers regard these preliminary attacks as a Raynaud phenomenon but not a true Raynaud disease. The point is a difficult one. It is true that in some cases of Raynaud's disease acrosclerosis does not develop, but on the other hand a careful and patient inquiry into these prodromal symptoms in cases of fully developed acrosclerosis leaves me in no doubt that the earlier symptoms are identical with those of Raynaud's disease. It seems reasonable to assume that long-continued and severe spasm leads to arterial thrombosis. There is evidence on this point from the pathologic picture of cervical rib[9] and of ergotism.[10] An arteriogram which was made by my colleague H. T. Simmons has a direct bearing on the question. A middle-aged man had suffered for nine years from severe Raynaud's disease and in 1933 began to show definite signs of sclerosis which became steadily worse. A cervicodorsal ganglionectomy on the right side gave complete relief for a few months, after which the condition recurred. In 1935, in spite of repeated trials with all kinds of treatment, the patient was so far reduced by constant pain and consequent insomnia that he begged for amputation of the hand. The hand was removed, and immediately after the operation injections of barium cream were made into the hand and roentgenograms were taken. These procedures showed that the arterial supply to the terminal phalanges was greatly reduced—it was in fact entirely abolished in the regions in the index finger and almost lost in the thumb.

From this it appears probable that the explanation in these cases of acrosclerosis is as follows: Long-continued and severe attacks of spasm cause thrombosis of the vessels. In cases of cervical rib and of ergotism this thrombosis begins in the small terminal vessels and spreads against the circulation to the larger arteries. Since the circulation is not

9. Telford, E. D., and Stopford, J. S. B.: Brit. J. Surg. **18**:557, 1931.

10. von Recklinghausen, F.: Handbuch der allgemeinen Pathologie des Kreislaufs und der Ernährung, Stuttgart, F. Enke, 1883, p. 349.

suddenly or grossly interfered with, massive gangrene does not occur, but a condition of fibrosis gradually develops. This fibrosis is the result of chronic subnutrition of the tissues. So far one is on sure ground; the rest is speculation, but one may be permitted to think that perhaps in this condition of undernourishment the ceaseless replacement of cells which constitutes life cannot take place and nature is reduced to the most simple and inexpensive type of process, i. e., the formation of fibroblasts. In this respect it is interesting to remember that an attempted culture in vitro of more highly organized tissue is likely to result in the formation of fibroblasts.

The treatment of acrosclerosis is difficult. It is clear that in the more advanced stages nothing that one can do is likely to have effect. I have submitted, in all, eight patients to cervicodorsal ganglionectomy, with results which on the whole are disappointing. In only two of these has the operation given increased mobility and brought about apparent arrest of the process. In these the condition was less advanced than in the others.

If it is true that in some cases Raynaud's disease is fated to pass into acrosclerosis, the solution must be in the earlier and more efficient treatment of the Raynaud's disease itself.

Professor Maitland made the inoculation tests on guinea-pigs, and Dr. Susman assisted in the preparation and interpretation of a large number of sections obtained for biopsy.

SENSITIVITY TO BOTH TRIVALENT AND PENTAVALENT ARSENICALS

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Patients who are hypersensitive to derivatives of arsphenamine are usually able to tolerate all pentavalent as well as trivalent arsenicals which do not contain an arsphenamine radical. Both Moore [1] and Stokes [2] pointed out that tryparsamide seldom leads to a recurrence of a dermatitis originally caused by a trivalent arsenical. The possibility that carbarsone, devegan or other arsenical preparations which are administered orally, rectally or vaginally may cause a recurrence of an arsphenamine dermatitis was not noted in reviewing the literature.

The following cases are reported to illustrate the hazards of prescribing any arsenical preparation for a patient who once had a dermatitis exfoliativa due to arsphenamine without investigating his sensitivity. The existence of hypersensitivity to pentavalent and trivalent arsenicals in the same patient was proved both clinically and by cutaneous tests in the first 2 cases, and the opportunity of observing these 2 cases led to the making of patch tests as a matter of routine in all cases observed at the clinic for syphilitic patients of the Los Angeles County Hospital in which eruptions had developed while arsenicals were being given. The other cases reported herein were discovered during this study. Although the reliability of patch tests is open to discussion, I did not feel justified in administering pentavalent arsenicals to these patients in order to establish combined sensitivity clinically.

REPORT OF CASES

CASE 1.—Mrs. E. D., aged 39, in 1928 underwent an operation for "a floating kidney and for pus in the kidney." The wound continued to discharge purulent material for nine months after the operation was performed. The patient became dissatisfied with her treatment and visited a second physician, who performed a Wassermann test of the blood. The reaction was 4 plus, and energetic antisyphilitic therapy was instituted.

She was given an injection in the arm and another in the hip each week. The first intravenous injection was followed by nausea, vomiting and severe abdominal pain that persisted for three days. Despite this warning, a second injection was given in the arm, and the patient suffered a recurrence of symptoms

From the Department of Dermatology and Syphilology, Los Angeles County Hospital.

1. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

2. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

even more severe plus a faint generalized pruritic erythema. The injections in the hip given later each week did not cause any untoward symptoms. A third intravenous injection was given one week after the second, and the patient suffered again, even more acutely than on the two previous occasions. In addition to the nausea, vomiting and abdominal pains, marked edema of the face, arms and legs appeared, and the eruption was more definite than on the previous occasion. Exfoliation soon developed, and even the nails and hair fell out during this process. The patient was confined to bed for three months and, according to her statement, was "unconscious" during the entire period. Her physician later informed her that she had "a facial paralysis and numerous convulsions."

Since then she has been treated in the syphilis clinic of the Los Angeles County Hospital and has received only intramuscular injections of bismuth preparations. On Dec. 20, 1935, she reported to the gynecologic clinic because of leukorrhea, and a diagnosis of infestation with Trichomonas vaginalis was made. Treatment was started with the vaginal instillation of 1 tablet of devegan.[3] One hour after the tablet had been inserted, the patient noticed a burning sensation when she urinated. Edema of the vulva soon developed, and this was of such severity as to cause marked pain when the patient sat down. She also complained of feeling feverish and of suffering from general malaise. On the following day she used another tablet, and an erythematous eruption appeared in the axillae and on the abdomen, arms, thighs and labia. This eruption was extremely pruritic. Two days later a fine exfoliation was noted in these areas. Treatment consisted of intravenous injections of sodium thiosulfate and dextrose and local applications of calamine lotion. Recovery was uneventful and complete nineteen days after the appearance of the dermatitis.

Patch tests were performed in March 1936. The patient had strongly positive reactions, consisting of a sharply demarcated pruritic erythematous area with superimposed vesicopapules, to neoarsphenamine, mapharsen, bismarsen, tryparsamide and devegan. Negative reactions were secured with arsenic trioxide, Ingram's four cacodylates,[3a] solution of potassium arsenite, phenobarbital, phenolphthalein and distilled water. The patient refused to cooperate in further percutaneous tests, as severe pruritus and generalized malaise developed after the aforementioned tests.

Case 2.—Miss M. N., aged 37, was studied with the permission of Dr. Norman N. Epstein of San Francisco. She was seen in 1928 at the Mount Zion Hospital in San Francisco, and a clinical diagnosis of the tabetic form of dementia paralytica was made. Both the blood and the cerebrospinal fluid showed serologic evidence of syphilis. After the sixth intravenous injection of neoarsphenamine, a typical exfoliative dermatitis developed which forced the patient to remain in the hospital for eight weeks.

She received no further arsenical treatment until 1932, when an intramuscular injection of 0.05 Gm. of sulfarsphenamine was administered and the dermatitis exfoliativa recurred. At this time she was in the hospital for six weeks.

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3. According to the Winthrop Chemical Co., Inc., "devegan consists of acetylaminohydroxyphenylarsonic acid [acetarsone] and a substance obtained by subjecting carbohydrates to a partial transformation by mild oxidation and hydrolysis. A small amount of boric acid is also present. Each tablet contains 0.25 Gm. (4 grains) of the arsenical constituent." The product has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

3a. The formula for Ingram's four cacodylates is: iron cacodylate, 0.02 Gm.; sodium cacodylate, 0.065 Gm.; strychnine cacodylate, 0.002 Gm., and sodium glycerophosphate, 0.065 Gm.

Later she received only preparations of heavy metals, given intramuscularly, and induced hyperpyrexia. However, in 1934 she was given 0.5 Gm. of tryparsamide intravenously, and a definite pruritic exfoliating dermatitis was noted the same night. This attack was comparatively mild, but the dermatitis was generalized and persisted for two weeks.

Cutaneous tests were performed one year later and showed that the patient was strongly sensitive to neoarsphenamine, mapharsen, silver arsphenamine, sulfarsphenamine, bismarsen, tryparsamide, acetarsone and carbarsone. She did not react to arsenic trioxide, solution of potassium arsenite, sodium cacodylate, iron cacodylate, phenobarbital, phenolphthalein, dinitrophenol, quinine, acetylsalicylic acid, aminopyrine, sodium amytal, sodium bromide, potassium iodide or distilled water. Scratch tests were also performed on this patient, and complete agreement existed between the results of these and those of the patch tests.

Case 3.—In Mrs. C. E. C., aged 28, an exfoliative dermatitis developed in October 1935, after her twelfth injection of neoarsphenamine. Manifestations in the skin began as a pruritic erythema that first appeared on the arms and then spread to the face and abdomen. Within two days the patient's entire body was involved in a scaling erythematous eruption. She also complained of nausea and of a sensation of chilliness. She remained in the Los Angeles County Hospital until Jan. 16, 1936, and at the time of discharge her skin was completely well although she had lost all of her hair and all her nails.

After this she was treated with bismo-cymol only. On April 23, 1936, patch tests were performed. Strongly positive reactions were secured with neoarsphenamine, mapharsen, sulfarsphenamine, bismarsen, acetarsone and carbarsone. Tests with distilled water, tryparsamide, devegan, Ingram's three cacodylates, solution of potassium arsenite and arsenic trioxide gave negative results.

On May 7 she reported to the clinic exhibiting a mild scaling pruritic exanthem that was most marked on the neck and face and in the cubital fossae. It was felt that this represented an early exfoliative dermatitis due to absorption of the arsenicals from the patch tests. The eruption subsided in about one week.

Case 4.—In Miss M. K., aged 19, a papular secondary syphilid developed in February 1935. She was treated with weekly injections of a bismuth preparation and of neoarsphenamine. After the seventh injection of the arsenical, a dose of 0.9 Gm. having been given, a number of small red pruritic papules developed on the dorsum of the right hand. However, she was given 0.6 Gm. of neoarsphenamine one week later, and a vesicopapular eruption developed on the face, arms and legs on the following day. This spread to involve the rest of the body and two days later became dry and scaling.

The patient was treated at the Los Angeles County Hospital for six weeks and was practically free from exfoliation when discharged on July 1. Patch tests were performed on May 7, 1936. Neoarsphenamine, mapharsen, sulfarsphenamine, bismarsen, acetarsone, carbarsone, devegan, solution of potassium arsenite and Ingram's three cacodylates produced strongly positive reactions, while tests with distilled water and tryparsamide gave negative results.

Case 5.—In Mrs. C. A., aged 38, a generalized pruritic papular eruption developed after the twelfth intravenous injection of neoarsphenamine. This soon developed into a typical exfoliative dermatitis, which was most marked and persistent on the neck and eyelids and in the cubital fossae and did not subside until after three months of treatment.

Patch tests made four months after the appearance of the dermatitis showed marked sensitivity to neoarsphenamine, sulfarsphenamine, bismarsen, tryparsamide and acetarsone. The reaction to mapharsen was weak but definitely positive.

Tests with distilled water, carbarsone, devegan, Ingram's three caccodylates, a solution of potassium arsenite and arsenic trioxide gave negative results.

CASE 6.—In Mr. V. A., a Filipino aged 40, a generalized vesicopapular rash developed in April 1933, twelve hours after his fourth intravenous injection of neoarsphenamine. The patient had also received four intramuscular injections of a bismuth preparation. Edema of the ankles and eyelids accompanied the process, and exfoliation appeared two days after the onset. He was treated in the Los Angeles County Hospital and was discharged in good condition after four months. Three months later another injection of neoarsphenamine was given in another clinic, and the dermatitis recurred. This eruption persisted for one month. Since then the patient has received only a bismuth preparation intramuscularly.

Patch tests performed in June 1936 resulted in markedly positive reactions to neoarsphenamine, mapharsen, sulfarsphenamine, bismarsen, acetarsone and carbarsone. The reaction to tryparsamide was weakly positive. Distilled water, devegan, Ingram's three cacodylates, solution of potassium arsenite and arsenic trioxide did not cause any reaction.

COMMENT

The fact that pentavalent arsenicals may cause a recurrence of an exfoliative dermatitis due to arsphenamine is of clinical significance. While most hypersusceptible persons are able to tolerate tryparsamide and related compounds without serious difficulty, the cases reported illustrate the necessity of exercising care in administering any preparation containing arsenic to such patients.

In general the pentavalent arsenicals display little toxicity for the skin. Their ability as a group to do serious damage to the optic nerve is well recognized, but otherwise their toxic properties are not marked.

Skoog [4] in 1925 reported a case in which a dermatitis developed after the injection of tryparsamide. The patient had had two attacks of exfoliative dermatitis due to arsphenamine during the preceding year. However, numerous instances have been recorded in which a patient tolerated tryparsamide without difficulty after a dermatitis exfoliativa due to arsphenamine.[5] Ebaugh and Dickson,[6] O'Leary and Becker,[7] Phelps and Washburn,[8] Robinson [9] and others have reported

4. Skoog, L.: Tryparsamide Therapy in Neurosyphilis, J. Missouri M. A. **22**:387 (Oct.) 1925.

5. Solomon, H. C., and Viets, H. R.: A Comparison of Tryparsamide and Other Drugs in the Treatment of Neurosyphilis, J. A. M. A. **83**:891 (Sept. 20) 1924.

6. Ebaugh, F. G., and Dickson, R. W.: The Use of Tryparsamide in the Treatment of General Paralysis, J. A. M. A. **83**:803 (Sept. 13) 1924.

7. O'Leary, P. A., and Becker, S. W.: Further Observations on the Treatment of Neurosyphilis with Tryparsamide, M. J. & Rec. **123**:305 (March 3) 1926.

8. Phelps, J. R., and Washburn, W. A.: Toxic Effects of Arsenical Compounds Employed in Treatment of Syphilis in the United States Navy, U. S. Nav. M. Bull. **28**:659 (July) 1930.

9. Robinson, H. M.: Fixed Dermatitis Due to Tryparsamide, Am. J. Syph. **17**:507 (Oct.) 1933.

instances of a mild dermatitis occurring after the injection of tryparsamide in patients who were not known to be hypersensitive to trivalent arsenicals. Bragman [10] noted a severe exfoliative dermatitis, and Robinson [9] and Kemp and Menninger [11] reported fixed exanthems after tryparsamide therapy. Silverston [12] noted the occurrence of onychoptosis after injections of tryparsamide.

Carbarsone is a closely related pentavalent arsenical that is administered orally or rectally for amebiasis. Reported instances of cutaneous eruptions due to this drug include cases of mild dermatitis,[13] of exfoliative dermatitis resulting in death,[14] of icterus and of edema.[15] Acetarsone, according to Stokes,[2] may give rise to toxic erythema, urticaria or severe bullous or exfoliative dermatitis. Hauptstein,[16] after treating 185 patients with devegan, reported that 9 suffered from local discomfort or pain of an itching and burning nature and that in 1 edema of the labia pudendi developed.

The rarity of epidermal complications during treatment with pentavalent arsenicals is demonstrated by a consideration of the following facts: Robinson [9] noted but 3 instances of mild dermatitis and 1 of fixed exanthem in the course of administration of 50,000 injections of tryparsamide; Phelps and Washburn [8] reported 1 case of mild dermatitis in the course of 6,933 injections of the same drug, while Ebaugh and Dickson [6] found the same number in the course of 1,000 injections. Anderson and Reed [17] used carbarsone in 330 cases, and no eruption appeared in any.

This work suggests that in cases in which an exfoliative dermatitis due to arsphenamine has occurred the routine use of patch tests before the administration of other arsenicals may aid in preventing serious accidents. While the sensitivity is usually to the arsphenamine radical, it may be to the arsenic atom (case 4). Case 1 demonstrates the fact

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10. Bragman, L. J.: Tryparsamide Dermatitis, Am. J. Syph. & Neurol. **18**: 308 (July) 1934.

11. Kemp, J. E., and Menninger, W. C.: Fixed Eruption Due to Tryparsamide, Am. J. Syph. & Neurol. **19**:195 (April) 1935.

12. Silverston, J. D.: Tryparsamide Therapy in Neurosyphilis, Lancet **2**:693 (Oct. 2) 1926.

13. Carbarsone, report of the Council on Pharmacy and Chemistry, J. A. M. A. **103**:258 (July 28) 1934; especially F. Smithies, quoted in council report.

14. Epstein, E.: Toxicity of Carbarsone: Acute Fatty Degeneration of the Liver, Exfoliative Dermatitis and Death Following Its Administration, J. A. M. A. **106**:769 (March 7) 1936.

15. Smithies.[13] Epstein.[14]

16. Hauptstein, P., quoted in A Remedy for Vaginal Infections, editorial, Lancet **1**:382 (Feb. 15) 1936.

17. Anderson, H. H., and Reed, A. C.: Untoward Effects of Anti-Amebic Drugs, Am. J. Trop. Med. **14**:296 (May) 1934.

that the arsenical need not be introduced into the body by the intravenous route in order to cause a reaction. The devegan was employed for its local effect only, but apparently sufficient absorption occurred to cause evidence of systemic and epidermal intoxication to appear. Theoretically, carbarsone given by mouth or by rectum may produce a similar reaction in a patient who is sensitive to members of the arsphenamine series. Case 3 illustrates a recurrence of a dermatitis exfoliativa after the local application of arsenicals to the skin (patch tests).

A real danger to the hypersensitive patient is the matter of contamination of the syringe. If neoarsphenamine and tryparsamide are given with the same syringe, there is a possibility that traces of the former may cause an exfoliative dermatitis during a course of injections of tryparsamide. Schoch [18] has demonstrated that ordinary cleansing methods do not remove all traces of the arsphenamines from a syringe. This hazard also exists if intramuscular injections of preparations of heavy metal are given with the syringes that are used for the arsphenamines. In these experiments new glassware was employed in making the saturated solutions or suspensions used in the tests. This was done in an attempt to eliminate all possibility of the presence of small amounts of drugs to which the patient might have been sensitized. Such persons are often extremely hypersensitive, and the most minute dose may be sufficient to cause a recurrence of a dermatitis.

SUMMARY

A report is made of the cases of 2 patients who were known to be sensitive to members of the arsphenamine series. Mild recurrences of dermatitis exfoliativa appeared after the intravenous injection of tryparsamide in 1 and after the insertion of devegan into the vagina in the other.

Four additional cases are reported in which the polysensitivity of the patients was demonstrated by patch tests only.

The danger of employing any arsenical, including devegan and carbarsone, in treating patients who are sensitive to the arsenical preparations used in antisyphilitic therapy is stressed.

450 Sutter Street.

18. Schoch, A. G.: Patch Test and the Element of Syringe Contamination in Arsphenamine Sensitization Dermatitis, J. A. M. A. **98**:1367 (April 16) 1932.

EXPERIMENTAL ARSPHENAMINE DERMATITIS

OBSERVATIONS ON ITS ALLERGIC NATURE, WITH SPECIAL ATTENTION TO THE SCHULTZ-DALE PHENOMENON

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This is the fourth of a series of studies on the nature of cutaneous idiosyncrasy to arsphenamine, as produced in guinea-pigs. In preliminary experiments,[1] made with both intradermal and intravenous injections, it seemed that a locally irritating effect following the second injection was a prerequisite, if a cutaneous flare was to result from a subsequent intravenous injection of neoarsphenamine. In a more recent, unpublished work this conclusion has been found to be false. Carefully controlled experiments on a series of twelve guinea-pigs demonstrated that true sensitivity had developed after but one intradermal injection, since a typical cutaneous flare resulted from a subsequent intravenous injection. The explanation of this variation in results was not immediately apparent. Attention was later called [2] to the fact that a diet low in vitamin C apparently increased cutaneous susceptibility to arsphenamine in the guinea-pig, while a diet high in vitamin C seemed to inhibit the cutaneous reactions, possibly by fixing the arsenic in the tissues in a "silent depot." Although conclusive proof could not be advanced, this inhibition was apparently effected through a decrease in cellular irritability rather than through an intermediate allergic mechanism. On checking back it was then found that the vitamin C content of the diet had been a variable factor in the initial experiment with intradermal and intravenous injections and that there had been a sharp increase in the intake of vitamin C between the initial intradermal and the subsequent intravenous injection, thus inhibiting the cutaneous reaction.

Numerous clinical observations seem to point to the conclusion that infections, particularly those caused by streptococci, staphylococci and some fungi, aggravate certain allergic tendencies and broaden the bases

From the Section on Dermatology, Department of Medicine, Royal Victoria Hospital.

1. Cormia, F. E.: Experimental Arsphenamine Dermatitis, Canad. M. A. J. **34**:272 (March) 1936.

2. Cormia, F. E.: Experimental Arsphenamine Dermatitis: The Influence of Vitamin C in the Production of Arsphenamine Sensitiveness, Canad. M. A. J. **36**:392 (April) 1937.

of existing allergic sensitivities. Assuming that arsphenamine dermatitis was possibly allergic, I attempted to estimate the influence of the products of infection on the incidence and the severity of the reactions to arsphenamine. The simultaneous use of neoarsphenamine and the Burnet staphylococcus toxin did not result in an increased severity of the reactions;[3] in fact, the guinea-pigs were even less susceptible than a previously tested group of normal guinea-pigs. The explanation of this phenomenon could not be found, but it is possible that it was due to an increase in the content of vitamin C in the diet. Actual infection in the guinea-pig by a streptococcus known to be virulent to guinea-pigs gave a similar result.[4] At present these experiments are being repeated; in addition, bacterial protein, the logical antigenic source of bacterial allergy, is being used in a control experiment.

Conclusive experimental evidence of a true allergic basis for cutaneous idiosyncrasy to arsphenamine has not yet been advanced. Experimental work in human beings,[5] with the exception of the early work of Frei and that of Nathan, Munk and Grundmann,[6] has proved disappointing. Nathan and his co-workers reported that they had produced sensitiveness with a second intradermal injection of arsphenamine. Occasionally a 1:1,000,000 dilution of neoarsphenamine, injected at the previously sensitized site, gave strongly positive local reactions. A few highly allergic reactions were noted in which the whole body became erythematous and urticarial. The nature of such a reaction, whether a cellular reaction or a vasomotor phenomenon, might be questioned. The Prausnitz-Küstner phenomenon, however, was not observed.

Schreiner and Ensbruner[7] obtained Prausnitz-Küstner reactions when the serum either of a highly allergic person or of a patient with

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3. Cormia, F. E.: Experimental Arsphenamine Dermatitis: Reaction to Arsphenamine in Normal Guinea-Pigs and in Guinea-Pigs Given Staphylococcus Toxin, Arch. Dermat. & Syph. **34**:107 (July) 1936.

4. Cormia, F. E.: Experimental Arsphenamine Dermatitis: The Influence of Infection on the Production of Arsphenamine Sensitiveness in the Guinea-Pig, to be published.

5. Cannon, A., and Karelitz, M.: Intradermal Tests in Relation to Arsphenamine Dermatitis: A Study Based on Two Hundred and Fifty-Six Clinical Cases, Arch. Dermat. & Syph. **29**:485 (April) 1934. Moore, J. E.; Woo, S.; Robinson, H., and Gay, S.: Reactions of the Skin Following the Intradermal Injection of Arsphenamine: Post-Arsphenamine Dermatitis, ibid. **23**:74 (Jan.) 1931. Schoch, A.: Arsphenamine Dermatitis: Attempted Sensitization to Neoarsphenamine and Further Observations on the Patch Test, ibid. **30**:672 (Nov.) 1934.

6. Nathan, E.; Munk, A., and Grundmann, H.: Ueber experimentelle Sensibilisierungs- und Allergieerscheinungen der Haut gegenüber Myosalvarsan, Klin. Wchnschr. **8**:1714 (Sept. 10) 1929.

7. Schreiner, K., and Ensbruner, G.: Weitere Beiträge zur Frage der allergischen Salvarsanhauterscheinungen, Arch. f. Dermat. u. Syph. **170**:61, 1934.

actual dermatitis was used. Birnbaum,[8] working with the serum of sensitized animals in human beings, was able to obtain positive results only with repeated intradermal injections. He stated that the positive cutaneous reactions did not conclusively prove an allergic basis for the dermatitis.

Recent workers [9] have stated that arsphenamine is a partial antigen and that the serums of sensitized guinea-pigs contains a hapten. When serum of sensitized guinea-pigs was injected intravenously into sensitized animals, instant death often resulted. These observations, while certainly suggestive, have indicated at the most that further work is necessary.

The present study deals with observations on the Schultz-Dale phenomenon in guinea-pigs sensitized to neoarsphenamine. The work was prompted by the recent report of Kallós and Kallós-Deffner,[10] who obtained positive Schultz-Dale reactions in sensitized guinea-pigs under certain conditions. They used actively and passively sensitized guinea-pigs, suspending the uterus of each animal in five different baths consisting, respectively, of (1) a 0.1 per cent solution of arsphenamine, (2) arsphenamine plus the serum of sensitized guinea-pigs, (3) arsphenamine plus a mixture of tapioca, (4) horse serum and (5) a solution of histamine hydrochloride. Positive contractions were obtained when the mixture of arsphenamine and guinea-pig serum was used. Histamine caused a contraction. Horse serum caused contractions in the uteri of animals actively sensitized to arsphenamine and horse serum or passively sensitized with intraperitoneal injections of serum from guinea-pigs that had been actively sensitized with horse serum and arsphenamine.

This report, while suggestive, raised certain questions. In the first place, histamine causes contractions of the normal uterus. The results with horse serum did not seem conclusive, since identical reactions would have occurred in normal animals used as controls. The baths containing tapioca can be disregarded, since the irritant effect of the tapioca did not give a positive result. The fact that arsphenamine alone did not cause a contraction was of interest, as were the positive contractions observed when serum from sensitized guinea-pigs and arsphenamine were used together. The assumption was that the ars-

8. Birnbaum, G.: Neuere Untersuchungen über die Salvarsanschädigungen der Haut (Kritischer Ergebnisbericht), Zentralbl. f. Haut- u. Geschlechtskr. **49**:97, 1934.

9. Jadassohn, W., and Schaaf, F.: Untersuchungen über den Mechanismus der anaphylakitsch-urtikariellen Reaktion (Schultz- Dalesche Versuche mit Haptenen), Arch. f. Dermat. u. Syph. **170**:33, 1934.

10. Kallós, P., and Kallós-Deffner, L.: Experimentelle Untersuchungen über Salvarsanallergie, Klin. Wchnschr. **14**:1074 (July 27) 1935.

phenamine caused an antigenic foreign protein reaction in the guinea-pig, and this foreign protein (in the serum), when combined with the irritant (?) effect of the arsphenamine, caused a positive, truly allergic reaction to the Schultz-Dale test. Unfortunately, no mention was made in that report of either controls with normal uteri or—what was equally important—of concentrations of serum in the uterine baths. Dale [11] pointed out that even Schultz' early work [12] was subject to the same criticism, for if a dilution of serum of less than 1:100 was used, even normal serum would cause a toxic reaction and contractions. This reaction, in contrast to the exhaustible type of truly allergic response characterized by one maximal contraction, was repeatable on a single uterus. According to Dale's work, the uterus after a single maximal contraction to the true antigen would not react again unless the uterus was first desensitized and then resensitized by prolonged contact with a concentrated antigenic solution. While the present work with arsphenamine cannot be compared directly to Dale's experiments with horse serum, the underlying principle is similar. Arsphenamine and serum from arsphenamine-sensitized guinea-pigs are at best doubtful antigens and could not be expected to cause maximal contractions. It is conceivable, then, that two or even three partial uterine contractions could occur and still be considered true reactions.

MATERIALS AND METHODS OF THE PRESENT STUDY

Young, nonpregnant female guinea-pigs weighing not over 300 Gm. were used for the study. Four of them were used as controls; eleven had previously been sensitized to neoarsphenamine by the two injection methods [13] and two others had been passively sensitized with serum from sensitized guinea-pigs. Young virgin guinea-pigs were used, since uteri taken from pregnant and older animals showed variable spontaneous rhythms. A few uteri showed inexplicable rhythms when placed in a normal oxygenated bath of Ringer's solution. These were discarded. The statement has been made that changes in rhythm may accompany different phases of the estrus cycle. Microscopic sections were taken from six unselected normal uteri, the contractions of which had previously been recorded on a revolving drum in the usual fashion. Dr. J. S. Henry, of the Royal Victoria Hospital, examined these sections and estimated the stage of the estrus cycle. When the data thus obtained were correlated with the uterine graphs no apparent relations were present. This factor was accordingly disregarded in the subsequent experiments. The original method of Dale was used. A standard Ringer

11. Dale, H. H.: The Anaphylactic Reaction of Plain Muscle in the Guinea-Pig, J. Pharmacol. & Exper. Therap. **13**:167, 1912.

12. Schultz, W. H.: Physiological Studies in Anaphylaxis: I. The Reaction of Smooth Muscle of the Guinea Pig Sensitized with Horse Serum, J. Pharmacol. & Exper. Therap. **1**:549, 1909-1910.

13. Sulzberger, M.: Hypersensitiveness to Arsphenamine in Guinea-Pigs: I. Experiments in Prevention and in Desensitization, Arch. Dermat. & Syph. **20**:669 (Nov.) 1929.

solution was used, both in the control solution and as a diluent for the neoarsphenamine, since the uterus loses tone and does not contract readily in a bath of physiologic solution of sodium chloride. There was no preliminary perfusion, since Dale obtained identical results in experiments with and without it. The guinea-pigs were killed by a blow on the head and then quickly bled, so that accumulation of histamine in the uterus after the injury would be prevented. The uterus was then washed thoroughly in Ringer's solution.

The single horn method was used, since the two horns contract identically and since a reserve horn would be needed in the event of a strong exhausting contraction of the initially used horn in any of the baths. The horn was first suspended in a bath of Ringer's solution at 38 C. The bath was then oxygenated until the uterus had assumed a characteristic low tonus, with a small, regular rhythm. The actual experiment was then begun.[14]

EXPERIMENT 1.—The right uterine horns of two normal, unsensitized guinea-pigs, each weighing about 250 Gm., were prepared as previously described and placed, in succession, in baths consisting, respectively, of (1) Ringer's solution, (2) Ringer's solution plus neoarsphenamine (1:10,000 dilution) and (3) Ringer's solution with neoarsphenamine and serum from normal guinea-pigs (1:100 dilution). No contractions were observed.

EXPERIMENT 2.—Two normal and unsensitized guinea-pigs, which weighed slightly over 300 Gm., were prepared, and baths consisting, respectively, of (1) Ringer's solution, (2) Ringer's solution and neoarsphenamine (1:10,000 dilution), (3) Ringer's solution with neoarsphenamine and serum from normal guinea-pigs (1:250 dilution), (4) Ringer's solution with neoarsphenamine and serum from sensitized guinea-pigs (1:250 dilution), (5) Ringer's solution with the serum of normal guinea-pigs and (6) Ringer's solution with the serum of sensitized guinea-pigs. No contractions were observed.

EXPERIMENT 3.—Seven guinea-pigs that had been previously sensitized to neoarsphenamine were prepared, and the six baths described in experiment 2 were used. The uteri were thoroughly washed in Ringer's solution after the third bath had been used. In five of the seven no contractions were observed. The sixth uterus contracted slightly in the second bath and a little more in the third and fourth baths. Neither normal nor sensitized serum alone produced contractions, but since neoarsphenamine and normal serum caused a contraction, the results were of only doubtful significance. The seventh uterus showed minor contractions to the second, third and fourth baths, but since the unused uterine horn reacted similarly to the bath containing normal serum, no significance could be attached to the reaction.

EXPERIMENT 4.—Four actively and two passively sensitized animals were used. The two latter were sensitized by injecting intraperitoneally 2 cc. of serum from guinea-pigs actively sensitized to neoarsphenamine. The following baths were used: (1) Ringer's solution with neoarsphenamine (1:10,000 dilution), (2) Ringer's solution with neoarsphenamine and serum from sensitized guinea-pigs (1:50 dilution) and (3) Ringer's solution with neoarsphenamine and the serum of normal guinea-pigs (1:50 dilution). The percentage of serum was increased, to establish the possibility of a nonspecific effect, while that of the neoarsphenamine was kept at one-tenth the strength used in the Kallós experiment. Contractions were observed in the uteri of but two of the first group of four

14. Only the interpretation of the graphs will be given, since the original tracings were lost and cannot be replaced.

guinea-pigs. In the first reacting uterus definite contractions were observed in the first three baths. The contractions in the second and third baths were probably caused by the toxic effect of normal serum, and curves made to represent the contractions in the first three baths could not be interpreted as indicating true allergy. In the other reacting uterus similar curves were encountered, contractions occurring in the first three baths. It was concluded that the cause of the contractions was the strong concentration of the guinea-pig serum. In the last two uteri neoarsphenamine alone caused small contractions, so minor that no definite conclusions could be drawn.

The first of the two passively sensitized guinea-pigs had fairly well marked uterine contractions in Ringer's solution, but once a base line was reached, no added contractions were seen when the test baths were used. The uterus of the second passively sensitized guinea-pig did not react to any of the test solutions.

CONCLUSIONS

In these experiments the Schultz-Dale tests were not conclusively positive in any guinea-pig. Minor contractions were observed in four of eleven actively sensitized animals, but since normal serum caused contractions in the same four, the results were of dubious value. No strong contractions, such as those recorded by Dale in his work with horse serum, were seen in any of the experiments. Contractions were obtained as easily with mixtures of neoarsphenamine and the serum of normal guinea-pigs as with mixtures containing serum from sensitized animals. Although no contractions were seen with any of the control subjects, the positive reactions were dubious and not considered true allergic phenomena. Any allergy which may have been present was of low grade at best, and its presence was denied rather than confirmed by the Schultz-Dale testing.

PYOGENIC RELAPSE AND SENSITIVENESS TO LIGHT IN CERTAIN DERMATOSES

INFLUENCE OF A FACTOR OF INTERCURRENT INFECTION

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For some time we have suspected that intercurrent infections, especially in epidemic waves, exercise a marked sensitizing influence in dermatoses with an underlying allergic or infectious-allergic complex. In the past year in our practice this rôle has been played, apparently, by an "influenzal" type of nasorespiratory, gastro-intestinal and general infection, the epidemic character of which is attested by a number of official reports and such analyses as that of Gover,[1] which indicated an epidemic prevalence approaching twenty times the normal expectancy in one of eleven outbreaks. We are not referring, be it noted, to the well recognized cutaneous complications of influenza, the toxic erythemas and so forth, familiar since 1890 and recently reviewed by Derbandiker.[2] The group of eruptions to be discussed here consists of pustular flares of eczematized ids, or infection-sensitization eruptions, both pyogenic and mycotic, and of pustular relapses in the course of acne and the seborrheic dermatoses after apparent cures of the dermatoses, often of years' standing. The course of a typical flare of this sort in acne consists of the appearance without warning within from two to four days after onset of the infection of a crop or burst of superficial pustules or a sudden deeper infiltration and purulent breakdown of previously inactive lesions, comedones or colloid cysts. Areas long clear

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1. Gover, M.: Influenza Mortality in the United States During 1936, Pub. Health Rep. **51**:1399 (Oct. 9) 1936.

2. Derbandiker, M. O.: Ueber grippöse Hauteffloreszenzen, Acta dermat.-venereol. **14**:175 (July) 1933.

or not previously involved are attacked as well as the principal active sites, and impetiginous characteristics develop easily. Diffuse erythematous flares of the levurid and streptococcid types, the recognized allergic extensions of the flexural mycoses (Darier-Ravaut-Ramel syndrome), were noted in 16 of 134 patients, suggesting the sensitizing and relapse-inducing action often attributed to relapsing sinusal infections in allergic diseases.

In an effort to explain the demonstrable increase and epidemic distribution, as well as the clinical pyococcic characteristics, of these eruptions, some significant literature was recalled. During the epidemic influenzal years from 1918 to 1920 there were numerous references to the sensitizing effect of the influenza or virus phase to subsequent invasion by pyococci. Chickering and Park [3] called attention to staphylococcic pneumonia as a frequent complication. Small and Stangl [4] isolated streptococci from most of their patients with pneumonia and found staphylococci and pneumococci in some instances. Staphylococcic empyema was a fairly common influenzal sequel in 1919; Ballin [5] and Ransohoff [6] noted it especially at the Cincinnati General Hospital, where pneumococci played little part. Levin [7] found empyema in 5 per cent, otitis media in 12 per cent and sinusitis in 10 per cent of children with influenza. Keeler [8] pointed out that pyogenic otitis media follows mild as frequently as it does severe influenza. Abscess of the lung is rated by Fishberg [9] as especially common and serious as compared with other infections of the respiratory tract following influenza. Burgess and Gormly [10] recognized in a more recent epidemic of mild influenza (1930) that there was a striking rise in the incidence of pneumonia and an

3. Chickering, H. T., and Park, J. H., Jr.: Staphylococcus Aureus Pneumonia, J. A. M. A. **72**:617 (March 1) 1919.

4. Small, J. C., and Stangl, F. H.: Epidemic Influenza at Cook County Hospital, J. A. M. A. **74**:1004 (April 10) 1920.

5. Ballin, M.: Empyema Following Influenzal Pneumonia, J. A. M. A. **72**: 335 (Feb. 1) 1919.

6. Ransohoff, J.: Empyema at the Cincinnati General Hospital During the Influenza Epidemic, J. A. M. A. **74**:238 (Jan. 24) 1920.

7. Levin, I. M.: Influenza and Its Complications in Children: Review of Eight Hundred Sixty Case Histories in Cook County Hospital, Inclusive of Epidemics of 1918-1919 and 1920, Internat. Clin. **2**:65, 1920.

8. Keeler, J. C.: Acute Otitis Media Complicating Epidemic Influenza, Pennsylvania M. J. **23**:325 (March) 1920.

9. Fishberg, M.: Pulmonary Sequels of Influenza, Am. J. M. Sc. **161**:365 (March) 1921.

10. Burgess, A. M., and Gormly, C. F.: Pneumonia in Relation to an Epidemic of "Mild" Influenza, with the Report of Three Fulminating Cases Apparently Due to Staphylococcus Aureus, New England J. Med. **202**:261 (Feb. 6) 1930.

increased tendency toward the fulminating type caused by Staphylococcus aureus, as in the 1918 epidemic. Thus it appears from the literature that there is a legitimate expectancy that epidemic influenza will predispose toward pyococcic systemic complications.

So far as the skin itself is concerned, one of us (J. H. S.) with other collaborators began in 1918 to accumulate observations on the effect of intercurrent and focal infections in prolonging or increasing the severity of arsenical and other forms of exfoliative dermatitis, in which a factor of sensitization is now generally recognized. He and Cathcart [11] noted the swing to pustular complications after the onset of a cold or of infection of the upper part of the respiratory tract in patients with previously mild exfoliative dermatitis. The interplay of infection and allergy, which may involve bacteria, fungi and chemical sensitiveness, was illustrated even better in a later study, undertaken with Kulchar.[12] The influence of intercurrent infection on the incidence and characteristics of so-called postarsphenamine jaundice has also had attention (Stokes, Ruedemann and Lemon [13] and Wile and Sams [14]).

Virus infection, however, while strongly suggested as the sensitizing agent for pyococci by the foregoing studies, is not necessarily the sole explanation for these cutaneous diseases. Pyococci themselves are now well recognized as responsible for such epidemic gastro-intestinal disorders as marked the onset of the disease in many of our patients and were an integral part of the recent "influenzal" waves. An editorial in *The Journal of the American Medical Association* [15] succinctly reviewed the principal studies in this field. Subsequently Terrell and Owen [16] reported a 30 case epidemic of staphylococcic diarrhea, and Jankelson and Massell [17] suggested that in 5 patients with ulcerative

11. Stokes, J. H., and Cathcart, E. P.: Contributory Factors in Postarsphenamine Dermatitis, with Special Reference to the Influence of Focal and Intercurrent Infections, Arch. Dermat. & Syph. **7**:14 (Jan.) 1923.

12. Stokes, J. H., and Kulchar, G. V.: The Infection-Allergic Complex in Arsphenamine Dermatitic Reactions, with Special Reference to Dermatophytosis, Brit. J. Dermat. **46**:134 (March) 1934.

13. Stokes, J. H.; Ruedemann, R., and Lemon, W. S.: Epidemic Infectious Jaundice and Its Relation to the Therapy of Syphilis, Arch. Int. Med. **26**:521 (Nov.) 1920.

14. Wile, U. J., and Sams, W. M.: A Study of Jaundice in Syphilis: Its Relation to Therapy, Am. J. M. Sc. **187**:297 (March) 1934.

15. Food Poisoning, editorial, J. A. M. A. **104**:1332 (April 13) 1935.

16. Terrell, C. O., and Owen, M.: Observations on Recent Epidemic Diarrhea, with Bacteriologic Studies, Texas State J. Med. **31**:204 (July) 1935.

17. Jankelson, I. R., and Massell, B. F.: Pyogenic Skin Lesions Accompanying Chronic Ulcerative Colitis: Report of Five Cases, Am. J. Digest. Dis. & Nutrition **3**:19 (March) 1936.

colitis the pyogenic lesions of the skin were direct metastases of the gastro-intestinal condition and involved the same organism. Barenburg, Levy and Grand,[18] on the other hand, in a study of infantile epidemic diarrhea, while recognizing the frequency of purulent otitis media, could find no pyogen in the stools and suggested a virus infection because of certain characteristics of the complicating pneumonia.

It appears, then, that an induced sensitization to pyococci, whether of virus or of pyococcic systemic (gastro-intestinal) origin, is a fair presumptive sequel of epidemic intercurrent infection such as that which occurred during the past year in the eastern part of the United States. Our own observations tend to establish this sensitizing phenomenon as a significant occurrence. During 1936 we observed 134 instances of an apparently direct relation of pustular flares to intercurrent infections such as the colds, grip, conventional influenza and the gastro-enteritic type of infection. The incidence in female subjects slightly preponderated. One third of the patients had infections of the upper part of the respiratory tract; one half had gastro-intestinal infection, and one fifth had grip. Relapses unexplained by other factors, such as diet, fatigue, negligence, ingestion of alcohol, nervous tension, contacts and climatic conditions, were observed, in order of frequency, in 81 patients with acne vulgaris and acneform eruptions, in 17 with a mycotic-pyogenic-allergic dermatosis, in 12 with chronic extensive eczema (neurodermatitis), in 6 with pruritis ani et vulvae, in 6 with dermatophytosis of the feet accompanied with dermaphytids and in a few with seborrheic, rosaceal or furuncular eruptions, an eruption caused by stasis or by a drug, lupus erythematosus or cheilitis.

It is notable as a first suggestion of the allergic character of this type of relapse that a marked trend toward familial pyogenic susceptibility was observed in the patients, as noted by Stokes and King[19] in their study of acne and seborrheic dermatoses. This pyogen-predisposed background appeared among patients with allergic eczema in 91 per cent, with dermatophytosis in 84 per cent, with acne in 75 per cent and with pyogenic-mycotic-allergic dermatosis in 70 per cent. A second suggestion of an allergic background for the phenomenon is the latent period, during which sensitization to the pyogenic or pustule-producing agent might take place. In 60 per cent of cases the outbreak began between the seventh and the eleventh day following the recog-

18. Barenburg, L. H.; Levy, W., and Grand, M. S. H.: An Epidemic of Infectious Diarrhea in the New-Born, J. A. M. A. **106**:1256 (April 11) 1936.

19. Stokes, J. H., and King, A. D.: Acne Vulgaris: Heredity in the Etiologic Background, Arch. Dermat. & Syph. **26**:456 (Sept.) 1932.

nized onset of the general infection. Leipner [20] observed a latent period of from eight to ten days preceding an epidemic outbreak of erythema multiforme in 30 of 56 boys in a school home, after mild coryza.

As in previous epidemics of influenza, the possible sensitizing influence of mild infection and the possibility that a carrier state without active or disabling symptoms might be followed by "flares" were suggested by 11 persons in our series who were not ill but were surrounded by persons epidemically seized by the infection, including members of their families and persons in the same boarding houses or offices. Close questioning, however (avoiding suggestion), often elicited evidence of an abortive attack of the disease, especially of the gastro-intestinal type. This took the form of abdominal cramps, in some cases followed by two or three large watery stools, a feeling of lassitude and even prostration, achiness and depression lasting for some days. In the more recent cases, pains in the shoulders and "neuritis" have been more conspicuous. It was equally observable that some patients with typical systemic seizures had no cutaneous relapses or flares, these seeming to be patients who had recently had fairly extended roentgen irradiation, which perhaps exerted some inhibitive effect.

The development of sensitiveness to light, which may be rated as an almost inescapably "allergic" phenomenon in this group, has a special interest. This manifestation developed in 4 of our patients, in association with either systemic or local pustular infection. For a number of years one of us (J. H. S.) has observed as an occasional, almost alarming, complication of extensive ultraviolet irradiation to the cutaneous surface the sudden development of an extreme reaction to a standard recorded dose in a series of exposures with one lamp. This reaction was at first blamed on technical variations in output or fault of the attendant, but it was finally suspected that marked sensitiveness to light, constituting almost a medicolegal hazard in treatment, could quickly develop under unknown circumstances. Ingestion of drugs not being involved, reasons for the phenomena remained a mystery which will be illuminated in part, perhaps, by 2 cases in this series, as follows:

CASE 1.—A physician under treatment with a Westinghouse S-1 sunlight lamp for a dyshidrotic-dermatophytic (?) dermatitis of the palms had reached a point at which he could tolerate an eighteen minute exposure at 5 inches (13 cm.) without reaction. About October 1 he sustained an attack of bronchitis, a condition which had attained epidemic prevalence in his practice. On the third day after onset of the pulmonary symptoms the dermatitis on the palms flared with fissuring, and his tolerance of a lamp of the same type fell to a point at which three minutes' exposure produced a severe burn. Since this sensitizing episode, his course has been much less favorable than before.

20. Leipner, S.: Beitrag zum epidemischen Auftreten des Erythema exsudativum multiforme, Dermat. Wchnschr. **101**:1178 (Sept. 21) 1935.

CASE 2.—A white woman with dermatitis involving the hands, the arms and the neck progressed favorably and rapidly under local and general irradiation from a quartz mercury vapor arc lamp for three minute periods at 30 inches (75 cm.) when the lamp had run for more than an hour before use for fully stabilizing its output. Five days before the latest exposure, grip developed, and the customary dose produced, both locally and generally, an acute exfoliative dermatitic reaction which required hospitalization.

In our series, excluding cases 1 and 2, two examples were observed as follows: A woman who had never exhibited sensitiveness to light, even to the sunlight at the beach in New Jersey, suffered clinically typical streptococcic dermatitis, which developed in both ears while she was in Maine (Mitchell [21]). Under exposure to sunlight the process extended terrifically and necessitated hospitalization and an allergic study, in which sensitiveness to phenol was identified. Three recoveries terminated in relapse on exposure to sunlight, and the patient is still severely sensitive to light, although her skin remains clear when she avoids even mild exposure to the sun. Another woman, who was not ordinarily sensitive to light, had lupus erythematosus which gave no evidence of a disseminating tendency. She was receiving without complication, gold sodium thiosulfate for the process. While nursing her child, who had coryza and diarrhea, then epidemic, she received an injection of 75 mg. of the drug, and on the second day thereafter a flaring dermatitis developed on the exposed areas of the face and neck, accompanied with malaise and achiness. This was not an exacerbation of the lupus erythematosus, and it subsided without leaving any lasting sensitiveness to light or any exacerbation of the original disease. It is suggested that the gold preparation and the infection acted together, as combinations of an arsenical preparation and an infection do, to cause a fleeting sensitiveness to light that determined the distribution of the dermatitis, which was exactly defined by the V of the dress and the neckline. Other examples appear in our series in which an interplay of factors, which sometimes makes it difficult to distinguish cart from horse, marked the flares of previously light-tolerant acne following short sharp exposures to New Jersey sunlight under conditions suggesting latent incubating or active intercurrent infection. In fact, so-called sun sickness has many of the characteristics of an infectious-allergic complex in which susceptibility to light and a pyogenic sensitivity with flare seem to be involved. The relation between light as a sensitizer to pyococci (an effect similar to "broadening of the allergic base"), pyococci as sensitizers to light and either or both as tied up with sen-

21. Mitchell, J. H.: Streptococcic Dermatoses of the Ears, J. A. M. A. **108**: 361 (Jan. 30) 1937.

sitivity to metals, such as nickel (Cormia and Stewart [22]), or to chemical compounds, such as sodium gold thiosulfate and the arsphenamines, deserves further observation. The possibility that the virus is the underlying sensitizer must not be lost sight of in such estimations, but its action may not be essential. Harkavy and Maisel [23] have clearly pointed out for infectious asthma how the entrance of an infectious element opens the way for sensitiveness to wholly new and even non-bacterial elements, such as feathers. It is conceivable that such base-broadening effects may extend on the skin to the assumption of allergic rôles by organisms which ordinarily are mere harmless saprophytes on the cutaneous surface or in its glandular or follicular structures.

We have performed as a matter of course certain statistical control studies on the subjects in the practice on which these observations are based. The peaks of pustular relapse were not synchronized with mere variations in the volume of practice. A well defined peak of pyococcic infections early in the fall recurs year after year, which suggests the possible pyogen-predisposing influence of summer, with camp-herding, large consumption of cold sweets and possible wholesale sensitization by sunlight. This wave is carried forward into the winter peak of pyogenic dermatoses perhaps determined by intercurrent infection, and in 1936 impetigo, influenza in the Philadelphia area and our pustular relapses reached their fall and their winter peak together. Using relapses in acne as a fair sample, and comparing the data for 1933 with those for 1936, we find that there were more pyogenic relapses by one-third in 1936 than the total of relapses from every conceivable cause in 1933.

It would seem, furthermore, that the spring peak of 1936, unique for that year, was closely associated with epidemic infection and that the winter peak is a more or less constant accompaniment of the systemic infections of the respiratory tract which are prevalent at that season. That the wave of infection of the respiratory tract is capable of influencing the pyogenic allergic dermatoses is suggested by our 1936 experience specifically.

Certain prognostic and therapeutic observations came from our experience: The sensitization, if such it was, induced by the intercurrent infection tended to subside, unless it was superposed on a previously highly allergic reactivity. In that event the patient was notably worse for a long period and repeatedly had relapses or was forced to remove himself to a new environment in order to recover. The temptation to resume or overprolong radiation therapy had to be resisted. The warm

22. Cormia, F. E., and Stewart, S. G.: Nickel Dermatitis: Report of Eleven Cases, Canad. M. A. J. **32**:270 (March) 1935.

23. Harkavy, J., and Maisel, F.: Infectious Asthma and Its Relationship to Chronic Sinus and Pulmonary Disease, J. A. M. A. **96**:1843 (May 30) 1931.

compress of potassium permanganate in an aqueous solution of 1:8,000 was found preferable for its effects to the continued use or resumption of derivatives of sulfur, resorcinol or quinoline, to which some patients seemed to become distinctly sensitive. The use of small doses of multiple strain staphylococcus toxoid seemed to be of some value in the more persistent complications.

SUMMARY

It appears from a study of the incidence of pustular relapses and pyogenic dermatoses in a typical dermatologic practice in comparison with that of regionally epidemic infections of the respiratory and gastro-intestinal tracts, that intercurrent infections, in part at least presumably of the virus type, predispose definitely to relapse and presumably to clinically pyogenic and partly pyogenic (acneform) eruptions. Such relapses show a tendency to occur in persons with familial or hereditary predisposition to pyogenic attacks, occur after mild as well as severe attacks of the intercurrent infection and may even be suspected of occurring in comparatively asymptomatic carriers, surrounded by patients with symptomatically active disease. Their onset tends to follow a period of incubation of from seven to eleven days, suggesting the development of an allergic or hypersensitive state; the development of such a state as part of an infectious-allergic complex is still further suggested in certain cases of relapse of primary pyogenic infection by the appearance of sensitiveness to light and apparently also of sensitiveness to both light and drugs.

These observations receive a certain amount of support from the literature. They are, we believe, of importance, as pointing toward an infectious-allergic background in pyogenic and pyogen-complicated cutaneous disease in general, and especially in acneform eruptions, of which our series is largely composed. In the etiology of cutaneous diseases we would thus add one more type of allergy to those of food and contact to which Cleveland White [24] has called attention, namely, allergy dependent on systemic, intercurrent and often seasonally or epidemically prevalent infection. The course of such sensitizations and relapses may be mild and transient, or it may be protracted and severe, depending probably in part on the allergic predispositions of the subject and in part on the survival after the acute attack of persistent focal or local infection, such as chronic nasorespiratory or gastro-intestinal disease. Therapists should be warned, when such relapses occur in patients who have had radiation therapy, against its reapplication as a mere surface attack on the condition.

24. White, C. J.: (*a*) Allergy in Diseases of the Skin, M. Clin. North America **18**:1253 (March) 1935; (*b*) Modern Treatment of Acne Vulgaris, ibid. **18**:1465 (March) 1935.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: Dr. Stokes asked me to discuss his paper if I did not find the facts set forth too unorthodox and particularly if I was not in agreement with the conclusions presented. I can now say emphatically that I am in agreement with these conclusions and that I can confirm the clinical observations of Drs. Callaway and Stokes. I have seen flare-ups of acneform dermatoses, of atopic dermatitis and of seborrheic dermatitis following intercurrent infections called cold or grip. I should like to warn—not Drs. Stokes and Callaway, because I am sure they have borne the point continually in mind, but other physicians observing such flare-ups—that bromides, iodides, barbiturates and other drugs taken in the presence of colds and grip are notorious for producing exacerbations of pyoderma and other dermatoses. It is essential to rule out the remotest possibility of ingestion of these drugs in accounting for such flare-ups.

However, the accuracy of the essayists' interpretation of the phenomenon here pointed out not only is based on clinical observations but has a large background of experimental confirmation. The flare-ups, or pyogenic relapses, consist, from the immunologic standpoint, of reactions or alterations of certain tissues, which are due primarily to one substance or agent and becoming activated through exposure to a different substance or agent.

One observes this phenomenon in other clinical manifestations, such as sensitivity to food and to pollen. There are patients who will exhibit sensitivity to certain foods only during the pollinating season of a pollen to which they are sensitive.

As Dr. Callaway has brought out, Dr. Cleveland White has demonstrated that flare-up of a dermatophytosis or id may occur in conjunction with the ingestion of certain foods to which the patient is sensitive, and Dr. Earl Osborne and others have shown that external irritants in conjunction with fungi may produce dermatitis when either one alone would not do so. These clinical observations and the torch-oil dermatitis manifest only in subjects with concomitant fungous infections, reported on on the present program by Dr. Adolph G. Kammer, are in accord with, and to a certain extent analogous to, the present observations of Drs. Stokes and Callaway.

But in addition to these clinical observations there is much experimental confirmation. For example, it has been shown that the site of an old tuberculin test can be made to flare up after distant injections of tuberculin and, more important still, in so-called nonspecific form after distant injections of trichophytin, oidiomycin, bacterial vaccines and even milk and other absolutely unrelated substances. I have seen the sudden simultaneous flare-up of many old, entirely healed sites of patch tests with several different substances in which the reaction appeared months previously after the ingestion or injection of some nonrelated drug or vaccine and even after the application at a distant site of a patch test with some other nonrelated substance.

A phenomenon which seems to have some relation to the matter under discussion and one that has been much talked about is known as the Shwartzman phenomenon. This phenomenon may be something different from that observed by Sanarelli many years ago. At any rate, it is only an example par excellence of such a dermatologically well known nonspecific effect, a flare-up in a site previously prepared by one factor and elicited by the additional, later injection of some entirely unrelated substance.

The second aspect of this report deals with the genesis of photosensitivity. One knows, especially well in dermatologic practice, that plants may produce

photosensitivity of the skin; fruits of the orange family—for example, the bergamot—and the fig are known cutaneous photosensitizers. Other plants which are notorious producers of photosensitivity are the euphorbia and other species that produce meadow-grass dermatitis (dermatitis bullosa et striata praetensis). There are also ingested and injected substances such as buckwheat, the barbiturates, derivatives of acriflavine, eosin, bengal rose and other drugs which produce cutaneous sensitivity to light. In addition, there are well known endogenous, autochthonous photosensitizing substances, such as certain of the porphyrins, and it may be assumed that anything which is capable of interfering in a certain manner with the natural metabolism of the porphyrins, for example through interference with hepatic function, may be capable of producing photosensitization. It is therefore possible that the intercurrent infections described by the essayists have an influence of this type, through altering the metabolism and producing autochthonous photosensitizing substances.

All dermatologists recognize that infections of certain types can produce photosensitivity. I have only to mention lupus erythematosus as an example.

There are probably certain more direct ways in which micro-organisms can produce photosensitivity. One of these is the actual production of photosensitizing substances by the micro-organisms themselves. For instance, fungi produce fluorescing compounds, and fluorescing compounds are likely to be photosensitizers. Still more direct is the relation between certain virus diseases and light. For instance, in smallpox one can prevent or reduce the eruption in many cases by preventing exposure to light, and I believe this is true to a lesser degree in chickenpox. There is, thus, in these virus diseases a definite influence on the appearance of the cutaneous manifestations attributable directly to the effects of light.

Another virus disease, herpes simplex, probably has something to do with photosensitivity in a certain number of cases. It is apparent in some persons that exposure to light breaks down the immunity or sensitizes the involved site to the apparently perennially present and lurking virus.

I see nothing in this paper which is in any way unorthodox, and I believe that it has been extremely important to hear this excellent record of clinical facts. I, though knowing the phenomena described, have often not borne them sufficiently in mind.

Dr. Samuel M. Peck, New York: This paper is of great importance because it adds to the understanding of many of the hitherto obscure causes for these flare-ups in allergic diseases.

All sorts of chronic dermatoses, including ids of various kinds, often completely disappear during an intercurrent infection, usually one such as erysipelas or carbuncle. Some observers have expressed the thought that the disappearing or marked amelioration of chronic dermatoses was due to the high temperature, while others have expressed the belief that the type of infection was mainly responsible. It was for this reason that thermotherapy and toxin have been used in treatment of many stubborn cutaneous diseases.

The question of desensitization to light has been shown by Miescher to be more on an anatomic-chemical than on an immunologic basis. When the skin is exposed to ultraviolet rays, the epidermis, especially the keratin layers, becomes thicker. In addition, certain chemical elements are built up in the upper layers of the skin, so that the combination of the increase in thickness and these chemical substances acts to filter the rays. As part of this mechanism, melanin is formed in the lower layers, so that a shield is built up for the delicate and important

structures in the basal layers, and in the parts of the cutis immediately below them. Here is an almost mechanical explanation for desensitization to light.

From a purely speculative point of view, sensitization to light may occur during an intercurrent infection in a patient in whom rise in temperature develops because of an accompanying marked desquamation of the skin. In this way those layers of the epidermis which have been formed because of photo-irritation are cast off. In addition, the formation of pigment might be suppressed during the course of an illness, and even the chemical constitution of the cells in the epidermis might be changed. Thus the mechanism which had been previously built up for protection from light might be lost.

The most important part of this paper has seemed to be the suggested explanation of the relationship between pustular infections, of the hands and feet especially, and foci of infection. A number of authors have maintained that such eruptions are ids—staphylococcids secondary to the primary infection in a diseased tonsil or tooth. In view of the work of Dr. Stokes and his collaborator, it may well be that, instead of being the primary focus for the eruption, the diseased tonsil or tooth helps to lower the patient's threshold for sensitization to organisms in the skin itself.

Dr. John H. Stokes, Philadelphia: Dr. Sulzberger's point about ingestion of bromides and iodides is well taken and is usually covered by our routine questioning. Emphasis should be laid on the necessity for careful quizzing of a patient in order to elicit the symptoms of the milder attacks of sensitizing infection. The importance of intercurrent infection first impressed us in connection with postarsphenamine jaundice, which in the large majority of cases has been shown by my study with Ruedemann and Lemon, subsequently confirmed by the observations of Wile and others, to be a possibly catarrhal infectious episode developing on a therapeutically predisposed background. The importance of the history of intercurrent and previous infection in the interpretation of dermatoses seems to us to be far greater than has been generally realized. It has been emphasized by Barber, who has said that no person who has ever had a severe infection is quite the same person thereafter. The patient comes out of it with a different set of reactivities and responses, many of them possibly included in the broad, sweeping, beautiful term "allergy." The broadening of the base of allergic susceptibility by intercurrent infection is therefore a constantly acting etiologic agent in dermatologic conditions and should be continuously in the minds of dermatologists as they deal with the daily problems of their patients.

The paper points a moral, perhaps, in that, amateurish though the thesis is to gentlemen as profoundly allergy conscious as the discussants, it none the less should encourage the ordinary physician to believe that he can do something investigative in his office and in his everyday practice. It is based solely on observation of man in a day when test tubes, animals and laboratories seem disconcertingly essential even to the slightest discovery. It is worth while, too, to point out that the next important job before the experimental investigator in this field is the production of controllable and controlled uniform infection in animals as a means of studying the behavior of their skins—a method the beginnings of which have been seen in the papers of Drs. Pillsbury, Kulchar and Sternberg in the past three years.

RINGWORM FUNGUS GROWING AS A SAPROPHYTE UNDER NATURAL CONDITIONS

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In a paper entitled "In Situ Cultures of Dermatophytes," Davidson and Gregory [1] stated that the cast-off hairs and epidermal scales of animals may be the medium for the spread of animal ringworm. They showed that when infected hairs are placed in a moist atmosphere the growth of the invading fungus continues with the production of a small saprophytic colony and the two usual types of accessory spores, aleuriospores and fuseaux, are borne in the manner normally observed in cultures made on artificial mediums.

These authors considered that although it is possible that the saprophytic stage of ringworm fungi may one day be observed under natural conditions on substances other than keratinized animal tissue, it may well be that such tissue is the most important natural medium on which ringworm fungi exist as saprophytes and produce spores capable of infecting human and animal hosts. The probability that these fungi spend their saprophytic stage on keratinized animal tissue rather than on other organic matter is strengthened by the fact that in such tissue they are almost entirely free from the competition they would encounter from fungi which grow rapidly on most carbohydrate-nitrogen mediums.

It is well known that ringworm infection spreads rapidly among healthy calves placed in sheds where infected animals have been previously housed. The frequency of tinea pedis and tinea cruris among persons frequenting infected swimming baths and gymnasiums is also well known. It is our contention that this rapid spread cannot be accounted for by the minute colonies which would result if the fungus grew as a saprophyte on the fallen infected hairs and scales only.

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This work has been made possible by the aid of an award granted by the Leverhulme Trust.

1. Davidson, A. M., and Gregory, P. H.: In Situ Cultures of Dermatophytes, Canad. J. Research **10**:373-393, 1934.

Although colonies of ringworm fungi on natural and synthetic culture mediums are readily seen by the naked eye, there is apparently no record of their having been observed under natural conditions. We considered, therefore, that a close examination of all possible natural mediums was necessary in order to decide the possibility of a saprophytic existence of fungi on material other than keratinized tissue. An occasion arose for conducting such an investigation when a heavy infection of calves was reported from a farm near Oxford, England, in April 1936.

On visiting the farm we found that there were seventeen calves in two large sheds with rough stone walls, wooden partitions and feeding troughs. The floor was covered with hay and a considerable amount

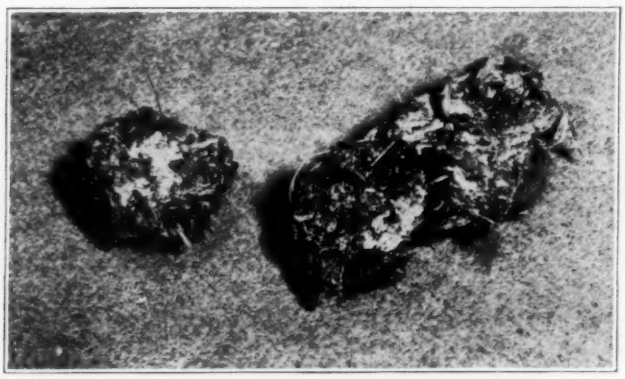

Fig. 1.—Light-colored colonies of T gypseum-asteroides growing on dung (×1.5).

of excreta, some of which had remained there possibly for three or four weeks. Numerous and conspicuous colonies of fungi, some reaching a diameter of about 3 cm., were present on the walls and excreta, but none was apparent on the woodwork.

It seemed likely that under these conditions the animals damage their skin on walls or woodwork and thus facilitate infection of their skin with a fungus. Removal of infected hair and scales might be effected in the same way and result in the dissemination of the organism, which possibly continues to grow as a saprophyte if conditions are suitable.

The infected animals were, as far as could be ascertained, perfectly healthy before they were confined in these sheds, but they had become heavily infected in the two months during which they had been living in them. The lesions were observed principally on parts anterior to the shoulders, the moist hairy areas near the nostrils, mouth and eyes being particularly affected.

Several samples of fungus were taken from the excreta and walls, but the specimens were members of the Mucorales and of the Aspergillaceae group, small growths of Pyronema domesticium and Trichothecium roseum being also observed.

Cultures of organisms of the Trichophyton gypseum group were obtained directly from hair and scales of the calves, and these were heavily contaminated with T. roseum. As T. roseum, P. domesticium and members of the Mucorales and those of the Aspergillaceae group are not pathogenic for guinea-pigs, we thought we might succeed in isolating the trichophytons by inoculating the contaminated material into animals. Hairs and scales were chopped into small pieces, mixed with hydrous wool fat for adherence and rubbed on an epilated scarified area on the backs of guinea-pigs. The lesions first appeared as erythematous areas about seven days after inoculation, but if the guinea-pigs were left unscarified the time between the inoculation and the appearance of the lesions was increased to ten days. Microscopic

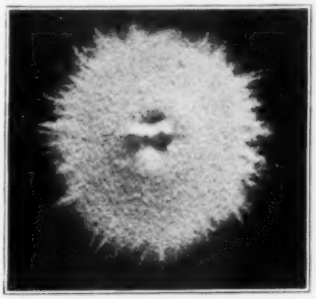

Fig. 2.—Fourteen day old colony of T. gypseum-asteroides growing on Sabouraud's proof medium (actual size).

examination of hair from this area revealed the presence of fungus of the Trichophyton ectothrix type, and the fluorescence test with Wood's filter gave negative results. The organisms cultured from the hair of the infected guinea-pigs on Sabouraud's proof medium corresponded to the Trichophyton gypseum-asteroides type, both macroscopically and microscopically.

After three months the sheds were reexamined and a much more comprehensive collection of fungi was made. At this time the sheds were occupied at night by horses, but these animals proved to be free from ringworm.

Of forty-seven samples taken from different parts of the shed, one, a powdery café au lait-colored colony on dry horse dung, was seen on microscopic examination to contain spiral hyphae, fuseaux of the trichophyton type and numerous aleuriospores. The color of the colony was found to be due to the absorption of brown pigment from the dung.

The fungus was isolated by the method of inoculation previously mentioned; lesions appeared after the same period (seven days), producing marked reactions. Cultures prepared from the hair of infected guinea-pigs produced colonies identical with those obtained with the material from calves.

Observation of animals in these two sheds during October disclosed the fact that when fourteen healthy calves were confined to the sheds every animal became infected within two weeks.

CONCLUSIONS

It is considered likely that fungi spread to suitable natural mediums from fallen infected hair, scales and detached spores, producing colonies larger than those which would form on hair or scales alone. The danger of other hosts becoming infected is greater owing to the increased amount of fungi available.

As far as we are aware, this is the first record of the discovery of a ringworm fungus growing as a saprophyte under natural conditions.

PITYRIASIS VARIOLIFORMIS ACUTA

REPORT OF A CASE OF EXTENSIVE INVOLVEMENT ASSOCIATED WITH BULLAE

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LOS ANGELES

Pityriasis varioliformis was first described in Europe by Mucha [1] in 1916. Wise and Sulzberger [2] recorded the first American case in October 1930, and Senear and Oliver [3] published the first comprehensive paper on the subject in this country in 1931. About 65 cases have been reported to date in the world literature. Complete bibliographies on pityriasis varioliformis have been given in papers by Juliusberg,[4] Senear and Oliver [3] and Gross.[5] It is the purpose of this report to describe a severe and extensive type of pityriasis varioliformis, presenting bullous lesions heretofore rarely described, which could be classified as pityriasis varioliformis bullosa acuta. Laboratory studies were made to determine, if possible, the presence of changes in the blood or its chemistry that could throw light on the etiology of the disorder. The extensive cutaneous involvement, the presence of bullae and the unusual clinical findings heretofore not recorded warrant a report of the following case:

REPORT OF CASE

Mr. J. W., a Jew aged 31, consulted me on May 26, 1936, complaining of a generalized itching eruption of three weeks' duration. There was no history of ingestion of medicaments or of exposure to external irritants before the onset of the eruption. He stated he had had no venereal infection. The patient's mother had renal tuberculosis fifteen years before, which necessitated a nephrectomy. One brother had active pulmonary tuberculosis. During the week preceding the onset of the eruption the patient had suffered from severe frontal headaches, lassitude, malaise, fever and chills. No nausea, vomiting or backache was present. The

From the department of dermatology, The Cedars of Lebanon Hospital.

1. Mucha: Arch. f. Dermat. u. Syph. **123**:586, 1916.

2. Wise, F., and Sulzberger, M. B.: M. J. & Rec. **132**:331 (Oct 1) 1930.

3. Senear, F. E., and Oliver, E. A.: Pityriasis Lichenoides et Varioliformis Acuta (Habermann), Arch. Dermat. & Syph. **23**:12 (Jan.) 1931.

4. Juliusberg, F., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, pt. 1.

5. Gross, P.: Pityriasis Lichenoides et Varioliformis Acuta (a Variety of Parapsoriasis), Arch. Dermat. & Syph. **23**:33 (Jan.) 1931.

patient had been vaccinated in childhood. The eruption had appeared in three crops of "pimples" at weekly intervals up to the time of the first examination. The patient complained of intense itching and burning at the sites of the lesions, severe enough to disturb his sleep.

The dermatologic examination revealed an intense generalized eruption that was especially pronounced over the trunk and upper extremities. The lesions were

Fig. 1.—Posterior view of the patient, showing the marked eruption on the back, with profuse hemorrhagic and necrotic lesions.

polymorphous and consisted of macules, papules, vesicles and bullae. Hemorrhagic and necrotic changes were present in all types of lesions. The bullae were predominant over the forearms. The papules were numerous along the lines of cleavage of the trunk, were round, waxy, yellowish brown and elevated and varied in size from that of a pinhead to that of a split pea. Some papules had minute vesicles at their tops. The bullae were formed from minute vesiculations that first appeared on the tops of papules. Several papulovesicles were on the

forehead and eyelids. The hemorrhagic bullae and vesicles were numerous over the flexors of the forearms and behind the knees. Pigmented and scarred relics of healed lesions were interspersed among the newer lesions. There was evidence of four distinct types of lesions in evolution and involution: macules, papules, vesicles and bullae. The palms and soles were involved with discrete pea-sized necrotic papulovesicles. At the time of the first examination the mouth and throat were normal; slight generalized adenopathy was present, and the temperature was 99.5 F. The diagnostic impression was that of pityriasis varioliformis of Mucha and Habermann with bullae, malignant syphilid or atypical variola.

Laboratory Examination.—The examination of the blood showed 90 per cent hemoglobin, 4,930,000 erythrocytes, 5,600 leukocytes, 68 per cent polymorphonuclear neutrophils, 2 per cent polymorphonuclear eosinophils, 0.5 per cent baso-

Fig. 2.—Appearance of the anterior aspect of the right forearm at the time of the first visit, showing the numerous bullae and vesicles with necrotic and hemorrhagic changes.

phils, 21 per cent lymphocytes and 8.5 per cent myelocytes. A stained smear showed the red cells to be regular in shape, normal in size and evenly stained. No nucleated red cells were found. The platelets appeared normal in number. Culture of the blood gave negative results.

Chemical examination of the blood showed, per hundred cubic centimeters, 25 mg. of nonprotein nitrogen, 12 mg. of urea, 2.7 mg. of uric acid, 89 mg. of sugar, 10.6 mg. of calcium and 495 mg. of chlorides as sodium chloride. The Wassermann and Kahn reactions of the blood serum were negative. A luetin test and an intradermal tuberculin test were negative after seventy-two hours. Urinalysis gave negative results.

A detailed description of the histologic picture of the macular, papular and vesicular lesions of pityriasis varioliformis would be a repetition of the reports of cases already recorded. The bullous lesions were the most interesting and unusual

features in my case, and the following description is of the histologic picture of a large bulla from the right forearm: The essential pathologic changes were in the epidermis and in the subpapillary layer of the cutis. The prickle cell layer was widened, and the rete cells showed marked ballooning and hydropic degeneration. Large cavities divided by septums were formed by the marked edema in the

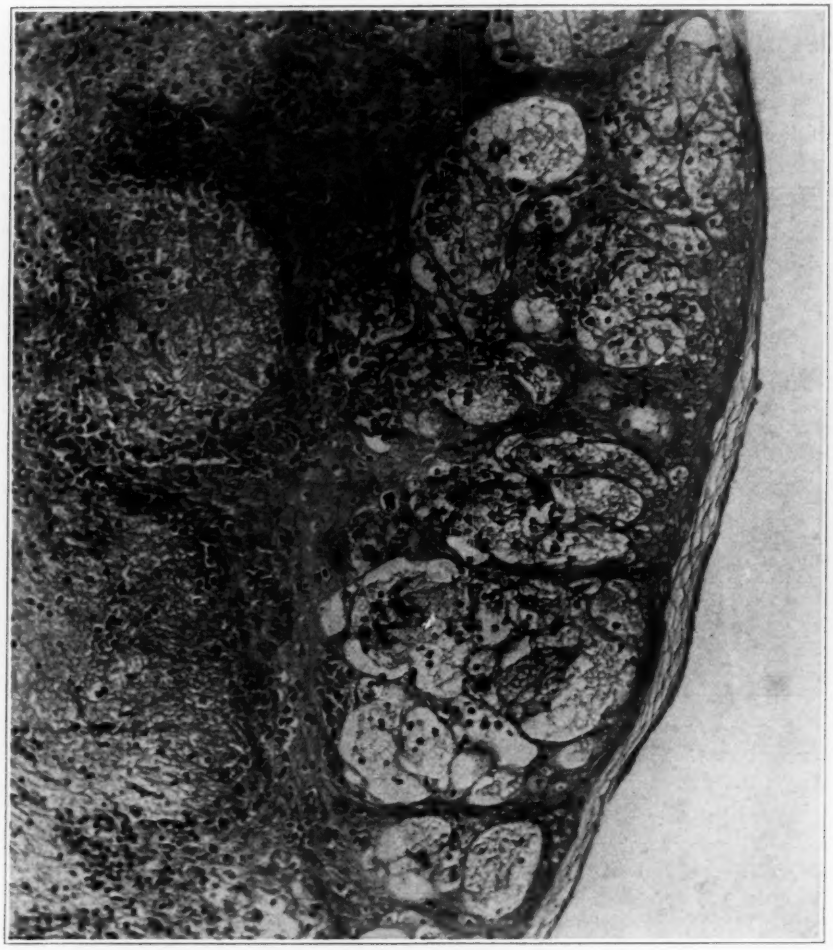

Fig. 3.—Low power magnification of a section of a bulla, showing marked ballooning and hydropic degeneration of rete cells with septums dividing the cavities in the papillary body.

papillary body. Hyperchromatic nuclei lay free in the cavities after disappearance of the cytoplasm. The cellular architecture of the rete layer was almost entirely destroyed. Lymphocytes and polymorphonuclear leukocytes invaded the entire epidermis and the upper part of the cutis. The usual distinct boundary line

between the cutis and the epidermis was obliterated by the marked edema and cellular degeneration.

Course and Therapy.—Between May 27 and Aug. 10, 1936, the patient received eighteen generalized suberythema doses of ultraviolet rays from an air-cooled quartz mercury vapor arc lamp. The eruption cleared slowly, with the appearance

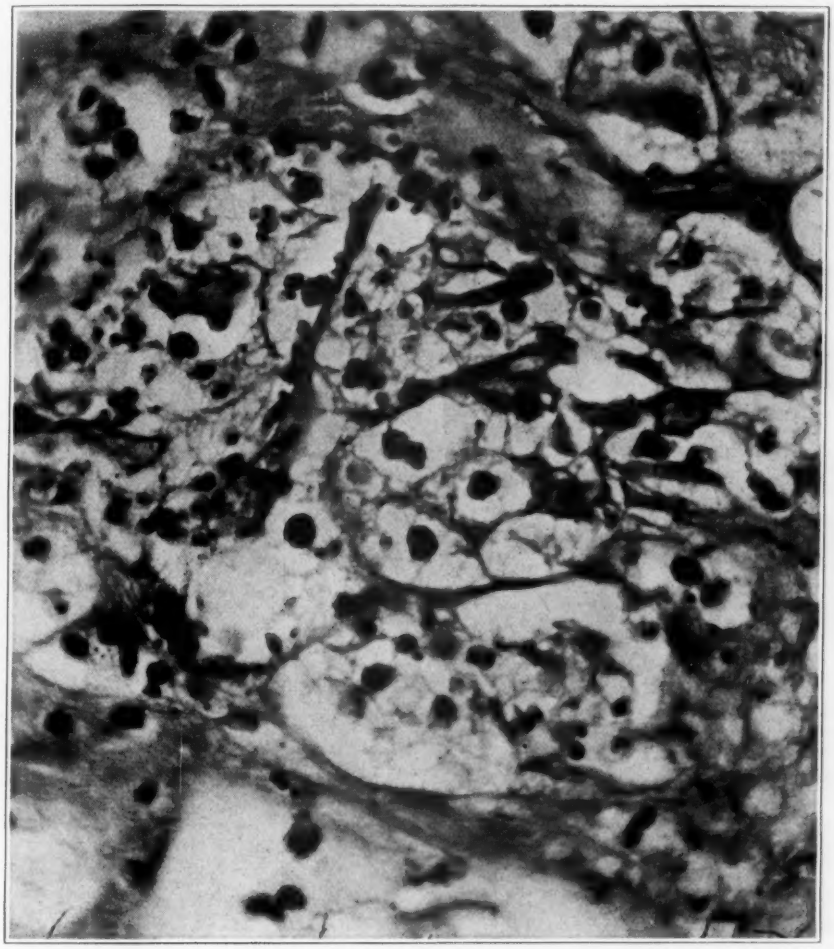

Fig. 4.—High power magnification, showing the destruction of the rete cells with nuclei lying free in the cavities in the papillary body. Polymorphonuclear and round cells have invaded the rete cell spaces.

of four additional crops of lesions. The bullae were predominant over the flexor surfaces of the forearms and the lower parts of the legs when the disorder was fully developed. Varioliform brownish pigmented scars remained at the sites of the necrotic and hemorrhagic lesions. The temperature ranged between 99 and

101 F. from May 26 until June 5, 1936, and then remained normal. At times severe chills occurred, and the patient suffered from malaise, anorexia and lassitude. The loss of weight was 10 pounds (4.5 Kg.). New lesions during this period appeared on the penis, the scrotum, the dorsa of the feet, the fingers, the toes, the palms, the soles, the upper part of the face, the lips and the hard palate.

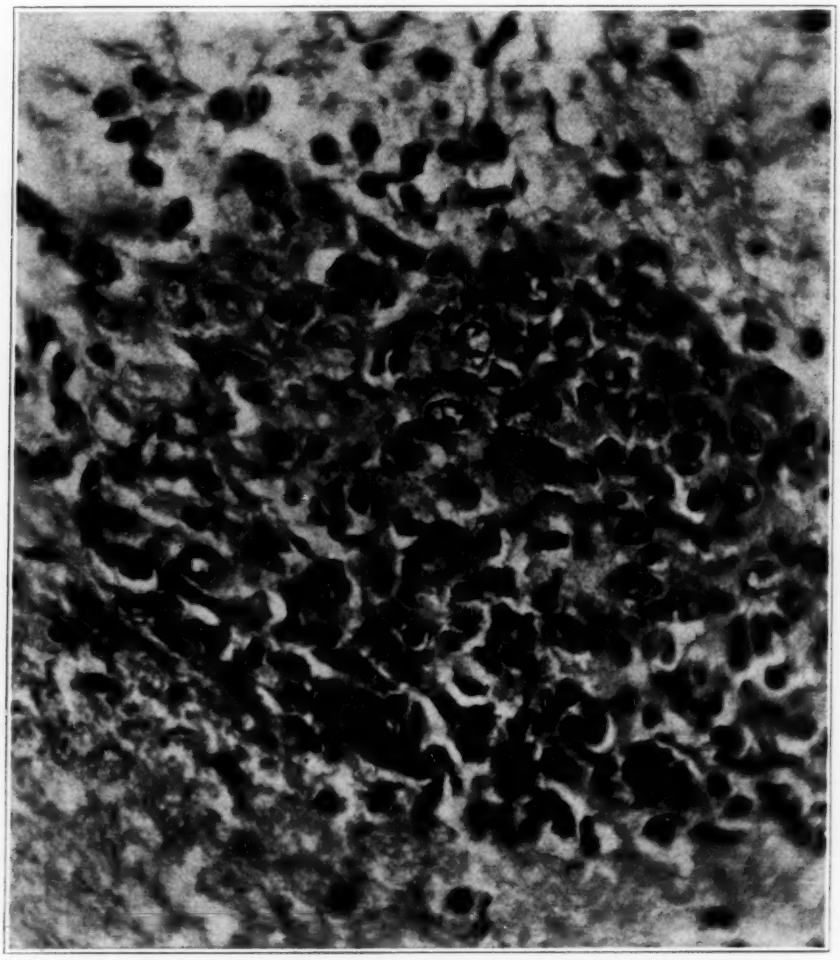

Fig. 5.—High power magnification, showing the degeneration of cells and edema at the border between the epidermis and the cutis.

The blood count on Aug. 10, 1936, showed 86 per cent hemoglobin, 4,890,000 erythrocytes and 5,800 leukocytes. The differential count showed 59 per cent polymorphonuclears, 34 per cent lymphocytes and 7 per cent monocytes. The color index was 0.88. Examination of a stained smear for changes in size and shape and staining of the red blood cells gave negative results. The platelets appeared normal in number.

COMMENT

Few authors reporting on pityriasis varioliformis have described extensive involvement and bullous formation such as those that occurred in my patient's eruption. No reports have emphasized the bullous lesions that may occur in pityriasis varioliformis acuta and that may tend to mask the true character of the eruption. Pruritus has been absent in nearly all reported cases, and this case is the third recorded in which it existed to a considerable degree. In fact, the absence of itching has been cited as characteristic of this disorder.[6] The presence of marked premonitory symptoms, such as fever, chills, severe headaches and malaise, for one week preceding the onset of my patient's eruption is unique. Heretofore, a few reports have mentioned a questionable malaise at the onset. The findings in my case point to a possible relation of pityriasis varioliformis to the exanthematous eruptive fevers and would indicate an infection, with a period of incubation and a premonitory stage.

Involvement of the palms, the soles, the eyelids and the hard palate was among the rarer manifestations of pityriasis varioliformis recorded here. The negative results of chemical analysis of the blood stress definitely the absence of any disturbance of the important chemical components of the blood during the course of the disease and corroborate similar reports.

1930 Wilshire Boulevard.

6. Crawford, S.: Pityriasis Lichenoides et Varioliformis Acuta: Report of a Case, Arch. Dermat. & Syph. **26**:990 (Dec.) 1932.

DERMAL RETICULOSIS OF OBSCURE NATURE

REPORT OF A CASE

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AND

K. G. KRISHNASWAMY, M.B.

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Lesions of the skin described under the general term lymphoblastoma by Mallory have received considerable attention in recent years. Having come across a case of this type presenting some peculiar features, we venture to place it on record. We have, however, preferred to use the term reticulosis for this lesion rather than lymphoblastoma, for reasons discussed in the text.

REPORT OF CASE

History.—S. R., aged 35 years, was admitted to the Mission Hospital at Narsapur, India, in August 1928, under the care of Dr. Clark. He complained of a swelling on the left side of the sternum. The swelling, 5 cm. in diameter, was slightly tender, without any ulceration. This was removed and sent to a laboratory and was diagnosed as lymphosarcoma. We tried to obtain the slide, but unfortunately it was not available. Later, he had some radium treatment at the General Hospital at Madras, India. In September 1933 he again sought admission to the same hospital, complaining of pain over the cheeks, a foul discharge from the nose and a small, growing nodule in the skin over the lower border of the right jaw. Examination showed that the nodule was the size of a large marble, without ulceration. The nodule was painless, had a firm, elastic texture and was freely movable over the underlying structures. The patient never suffered from itching. The scar at the site of the original tumor was clearly visible and measured 7.5 by 2.5 cm., extending from the left parasternal line at the level of the third rib to the middle of the left clavicle.

Besides the nodule over the jaw, there were a number of slightly raised copper-colored areas of various sizes. One of these, about 2.5 cm. in diameter, was situated in the third left intercostal space. Another was found in the second right intercostal space and measured 1 cm. in diameter. There was a small thickened patch of skin just outside the latter. On the inner side of the right nipple, there was a small thickened patch 1 cm. in diameter. Besides these, on the upper part of the abdomen just below the xiphisternum there was an area of purplish discoloration 6 cm. in diameter. All these patches showed definite thickening. There was neither scaling of the epidermis nor ulceration.

There was no enlargement of the lymph nodes, spleen or liver. Examination of the blood showed 5,200 leukocytes, of which 60 per cent were polymorphonuclears, 30 per cent lymphocytes, 2.8 per cent eosinophils and 7.2 per cent monocytes. The patient looked anemic, but the red cells were not counted.

From the Department of Pathology, the Medical College.

Histologic Examination.—The section of the nodule over the right jaw showed, under low power of the microscope, skin overlying masses of cells which extended at some places up to the epithelium but did not actually invade it. The cells were of two main varieties: large pale cells and small round dark-staining cells. The former were much more numerous than the latter. The small round cells were irregularly distributed and occurred in dense collections in some parts of the sections. Occasionally, the arrangement of the dark-staining cells was very striking; they formed a thin layer at the periphery of the spherical mass of large pale cells, presenting the appearance of a lymph follicle (fig. 1). The greater part of the growth was separated into irregular areas by bands of fibrous tissue.

Higher magnification (fig. 2) revealed a great variety of cells, which differed in size, shape and structure. The following types of cells were observed:

1. Large cells with an oval, pale nucleus closely adjacent to the surface of the argyrophil fibers occurred. The protoplasm was scanty, the outlines not distinct.

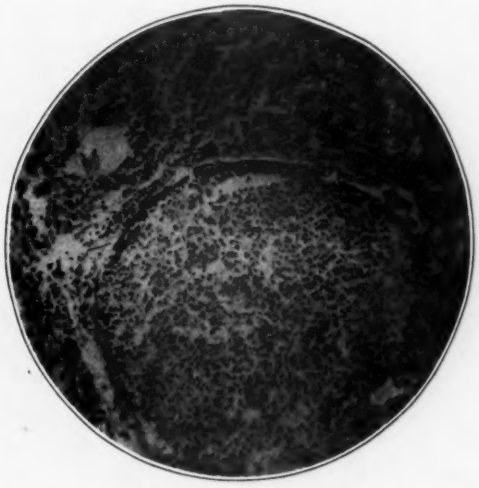

Fig. 1.—Section showing the follicular arrangement of cells, with a narrow rim of lymphocytes.

The cells probably correspond to what Maximow called reticular syncytial cells. These were not numerous.

2. Large stellate or spindle-shaped cells with more or less abundant protoplasm were seen. The nucleus was large, vesicular, pale and oval and contained a small quantity of chromatin. These cells were the reticular cells which showed evidence of phagocytosis and were abundant. Some of these cells were closely adherent to the reticular fibers, but others, which were more rounded, were found free (macrophages).

3. Besides these cells, there were in the meshes of the reticulum a number of mononuclear cells of various sizes. They possessed relatively large nuclei with various amounts of cytoplasm and could be divided into large, medium and small lymphocytes.

Mitotic figures were numerous and were especially observed in the large lymphocytes and reticular cells.

4. Eosinophil cells were fairly abundant and irregularly distributed.

5. Giant cells were also occasionally seen. Some of these were mononucleated and about twice the size of a large lymphocyte. Others were many times larger and were multinucleated. Their nuclei were vesicular and heaped together, and the outline of the cell was irregular. The structure of these cells bore some resemblance to that of a megakaryocyte (fig. 3).

Sections stained by Foot's[1] silver impregnation method revealed a definite increase in the argyrophil fibers (fig. 4).

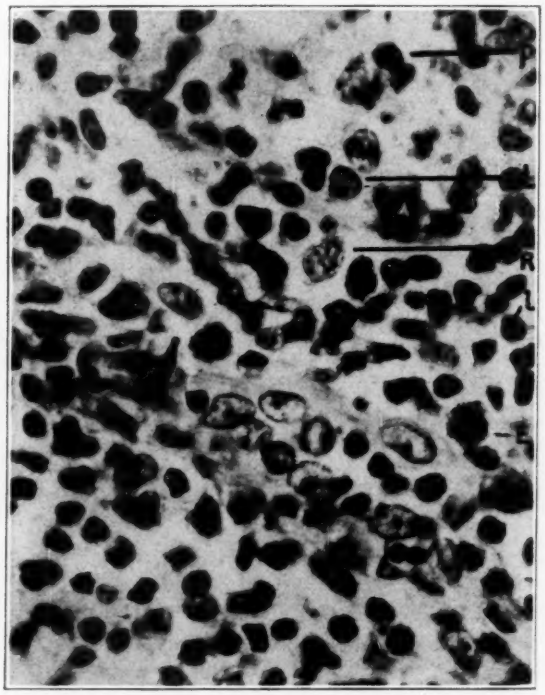

Fig. 2.—The section shown in figure 1 under high magnification, revealing the various types of cells—reticular cell *R*, eosinophil cell *E*, small lymphocyte *l*, large lymphocyte *L* and plasma cell *P*.

In order to study the earlier changes occurring in this condition, a bit of the thickened patch of the skin on the inner side of the right nipple was removed at our suggestion. This section showed skin with subcutaneous tissues which were infiltrated with cells arranged in groups widely separated from one another. In a few places, the cellular infiltrate was almost in contact with the cutaneous epithelium. The sweat and sebaceous glands were surrounded by collections of

1. Foot, N. C., and Menard, M. C.: A Rapid Method for the Silver Impregnation of Reticulum, Arch. Path. **4**:211 (Aug.) 1927.

cells, which, however, did not actually invade these structures. A striking feature of the section was the structural arrangement of the cells, which bore a close resemblance to a lymph follicle. The central area of these follicles was occupied by large pale cells, with abundant cytoplasmic processes, and the periphery consisted of a thin rim of compact mass of dark-staining round cells, i. e., small lymphocytes. The small lymphocytes were relatively few and were almost entirely confined to the edge of the follicles. They formed a conspicuous narrow band of deep-staining cells which outlined the periphery of each follicle. The giant cells and eosinophil cells were very scanty and could be observed only after a long and careful search. A great many of the cells were found in association with the adventitia of the blood vessels, and the impression was gained that they had arisen

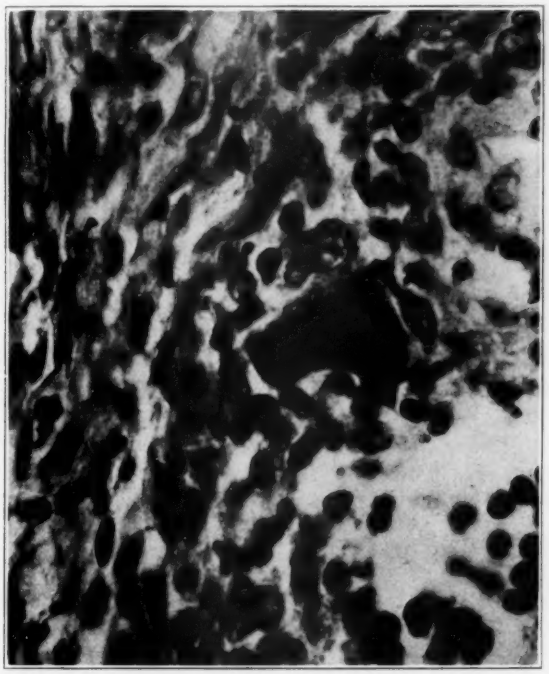

Fig. 3.—A multinucleated giant cell, reticular cells and lymphocytes.

in this zone (fig. 5). On July 22, 1935, about two years after we first saw the patient, we received a small nodular growth from the skin roughly ½ inch (1.3 cm.) in diameter and white, with the skin intact and without ulceration. This was removed from a site immediately posterior to the previous growth, overlying the horizontal ramus of the inferior maxilla. It had the same histologic picture as the previous section, except that the lesion appeared to be more extensive, though without any invasion of the epidermis. The lymphocytic zone surrounding the masses of pale cells was comparatively thin on account of increase in the number of reticular cells and large lymphocytes. No tubercle bacilli were seen in the sections.

Diagnosis.—The diagnosis was dermal reticulosis of obscure nature.

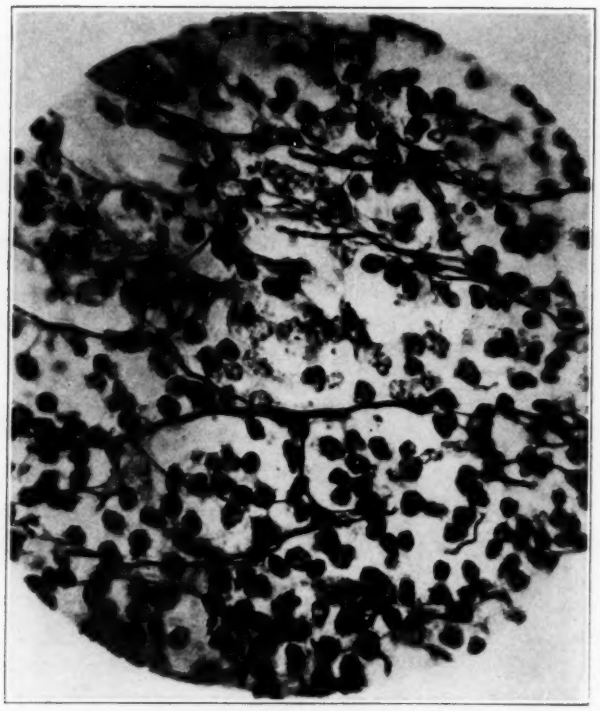

Fig. 4.—Photomicrograph of a section stained by the Foot-Menard silver impregnation method. Note the increase in argyrophilic reticular fibers and their relationship with the cells.

Fig. 5.—Localization of the cells around blood vessels and sweat glands.

COMMENT

From the clinical standpoint, the important feature was the formation of nodules in the skin, which first appeared as small thickened patches. These increased in size and became raised and appeared to form definite nodules, but there was no itching or ulceration. The patches and the nodules were not covered with scales. It would have been impossible to classify this condition without microscopic examination of the skin. Even with this examination, it was difficult to determine the real nature of the lesion and to make a definite classification. Indeed, three experienced pathologists to whom the sections were sent gave different opinions. As already stated, it was diagnosed as lymphosarcoma in a laboratory in India. We are not in agreement with this diagnosis for various reasons, provided of course, the histologic appearance at that time was similar to the present one. The other pathologist, while agreeing with the diagnosis of Hodgkin's disease, did not think there were sufficient grounds for regarding the malady as primary Hodgkin's disease of the skin. Our original opinion was that it was Hodgkin's disease with primary involvement of the skin. This opinion was based on the pleomorphic cell picture with giant cells and increase of reticular fibers and the absence of any obvious involvement of the lymph nodes in any part of the body or of the spleen. But the giant cells were not of the Sternberg type, with densely staining nuclei. Moreover the cellular infiltrate, though actually lying in contact with the cutaneous epithelium, does not actually invade it. We have not been able to keep the patient under observation and are therefore unable to say what the ultimate fate of these nodules will be. But our impression is that they grow very slowly, so slowly indeed that their growth cannot be appreciated. The third pathologist was of the opinion that it was a granulomatous lesion of a reticulo-endothelial type and that there were very few grounds for considering this as primary Hodgkin's disease of the skin.

Histologic examination revealed the presence of a polymorphous cellular infiltrate, the predominating cells of which appeared to be large mononuclears. Small lymphocytes and giant cells were also present in the specimens. There was an appreciable increase of fibrous tissue. In a few places a tendency to reproduce more or less the structure of a lymph follicle was distinctly noticeable. Some of the mononuclear cells showed ingested particles. While the predominating type of cell was the reticular cell, as shown by the presence of delicate cytoplasmic processes and phagocytosis, there were also intermingled with these cells a few large and medium-sized lymphocytes. The microscopic picture was extremely varied. This pleomorphism is suggestive of Hodgkin's disease, but for reasons stated before this view cannot be accepted. Reference must, however, be made to the growing tendency to regard the diseases included under the terms lymphogranuloma, lymphosarcoma,

pseudoleukemia, lymphatic leukemia and mycosis fungoides as genetically closely related. Mallory [2] suggested the term lymphoblastoma for the entire group. Warthin [3] stated that these diseases are variable expressions of lymphoblastoma, the different clinical forms partly depending on the organ or tissue involved and the state of differentiation and partly resulting from the transformation of one type into another and the occurrence of transitional forms. A great number of authors have adopted the view that these conditions are true neoplasms and are genetically closely related.

The earliest lesions of Hodgkin's disease and mycosis fungoides present such similar histologic pictures that it is extremely difficult to separate them definitely. For example, cellular pleomorphism is a prominent feature of both. Giant cells resembling Sternberg cells may be present in the premycotic stage of mycosis fungoides. In a section taken during the early stage of the process in this case the giant cells were extremely few, while in the more advanced lesion they were greatly increased in number, protoplasmic detritus was not found and the cell picture was pleomorphic. We believe that on account of the extreme difficulty of exact determination of the real nature of the lesion at such an early stage, the term dermal reticulosis would be most satisfactory.

The lesion could not be classified as a frank neoplastic process because of the pleomorphism of the cell picture, the absence of malignant quality of the cells and the freedom of the epidermis from infiltration even in the more advanced lesions. The presence of mitoses is not of much significance, as these are also very common in proliferating large and medium sized lymphocytes.

In leukaemia cutis of the lymphatic variety, the cellular infiltrate has a more uniform character, being composed almost entirely of lymphocytes, with an occasional mitosis. The absence of enlarged lymph nodes and of a leukemic blood picture is against a diagnosis of leukemic lymphadenosis. Much importance, however, cannot be attached to these observations, as cases have been recorded in which the glands became enlarged with or without a leukemic blood picture late in the course of the disease. Rössle [4] recently described two remarkable cases. His first case did not present much difficulty in diagnosis because the leukocyte count was 97,000, with 70 per cent lymphocytes. The only remarkable feature of this case was the absence of enlargement of the lymph nodes. His second case is of great interest, as the findings were unusual. A woman aged 61 years had recurrent attacks of some cutaneous con-

2. Mallory, F. B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914.

3. Warthin, A. S.: Ann. Surg. **93**:153, 1931.

4. Rössle, R.: Lymphoid Leukemia Without Involvement of the Lymph Nodes, Virchows Arch. f. path. Anat. **275**:310, 1930.

dition on the legs for three years. A diagnosis of mycosis fungoides or premycotic erythroderma was at first made, but in course of time the typical blood picture of lymphatic leukemia developed, and the cutaneous lesion was diagnosed as leukaemia cutis. There was no evidence of lymphoid hyperplasia of the lymph nodes, the spleen or the bone marrow on histologic examination of tissues removed at autopsy. Under the skin were found areas of cellular lymphoid tissue bearing a close resemblance to lymph follicles. A noteworthy point is that the cutaneous condition could not be diagnosed correctly until after the development of the leukemic blood picture. Until the final outcome of the condition is known, the exact nature of the lesion in our case must remain undetermined. If there is an opportunity of examining the patient again we shall certainly make another report if any unusual signs and symptoms develop.

Naturally the most interesting question concerns the origin of the cells present in the lesions described. Mention has already been made that in the earlier lesions the proliferating cells were found in the neighborhood of the blood vessels, and the histologic picture gave the impression that these cells had taken origin there. According to Maximow,[5] not all the mesenchymal cells become transformed into fibroblasts, so that many remain in an undifferentiated embryonic state in the adult connective tissue, especially near the blood vessels. These cells possess unlimited potentialities for development and in response to suitable stimuli produce through proliferation and progressive development new cell types—reticular cells, lymphocytes and the cells of the myeloid series. It appears that in our case, under the influence of some stimulus, the nature of which cannot be determined, reticular syncytium around the cutaneous blood vessels has given rise to the various types of cells, resulting in a pleomorphic picture. From a review of the relevant literature it appears that the question of relationship between cutaneous lymphogranulomatosis and mycosis fungoides is still unsettled. Fraser [6] traced the cells of mycosis fungoides to the reticular cells of the papillary layer of the skin. On the basis of Maximow's view it would be more nearly correct to say that the cells are derived from the reticular syncytium and not from the reticular cells, as the latter are differentiated and are not capable of producing other cell types. In the lesions of Hodgkin's disease of the skin and other related conditions it appears logical to assume that the cells are derived from the reticular syncytium and that the ultimate outcome depends on the line of differentiation of the proliferating cell and the acquisition of neoplastic characters.

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5. Maximow, A. A.: Text Book of Histology, Philadelphia, W. B. Saunders Company, 1930.

6. Fraser, J. F.: The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Arch. Dermat. & Syph. **11**:425 (April) 1925.

In Hodgkin's disease of the skin, for example, the stimulus for proliferation acts on the reticular syncytium, the root cell of the hematopoietic tissue. This is followed by differentiation, partial or complete, in all directions, with the production of a pleomorphic cell picture characteristic of Hodgkin's disease.

A similar stimulation of the reticular syncytium also occurs in mycosis fungoides, but this is followed by differentiation into lymphocytes, which forms so prominent a feature in the later stages that the cell picture comes to consist almost entirely of lymphocytes. The nuclear fragmentation of the tumor stage may depend on the increased activity of the irritant.

In lymphosarcoma of the skin also, one may imagine that the initial stage begins with hyperplasia of the undifferentiated reticular syncytium accompanied by differentiation into large and small lymphocytes. This lymphocytic proliferation may in favorable but as yet undefined circumstances lead to excessive and neoplastic growth.

Hyperplasia of the reticular syncytium with differentiation into lymphocytes also occurs in leukaemia cutis of the lymphatic variety, but the cells do not attain the malignant neoplastic characters of lymphosarcoma.

While the initial reaction in this group of diseases is a proliferation of the reticular syncytium, the ultimate results vary greatly, and thus these conditions come to present very different clinical and histologic characters. Whether differentiation of the root cell will occur in all directions, as in the case of Hodgkin's disease, or in only or mainly one direction, as in the case of lymphadenosis, or whether the proliferating cells will assume neoplastic characters or the progress of the lesion will be made too slowly for it to reach the stage of any of the well recognized type of the aforementioned lesions may be related, partly at least, to the nature of the irritant and the immunity of the host. If this conception of the origin and development of these conditions is adopted, their close relationships can readily be understood. In a recent paper Symmers[7] expressed the view that mycosis fungoides is neither a clinical nor a histologic entity. According to him, the histologic alterations in the tumors and tumor-like growths in the skin may be of three distinct types: (1) that of Hodgkin's disease, (2) that of a reticulum cell sarcoma and (3) that of lymphosarcoma. He found it difficult "to reconcile three such divergent histologic types with one and the same disease." We are conscious of the difficulties in the exact labeling of the many pathologic types of lesion of the reticulo-endothelial system

7. Symmers, D.: Mycosis Fungoides as a Clinical and Pathologic Nonexistent, Arch. Dermat. & Syph. **25**:1 (Jan.) 1932.

met with. Besides the well recognized lesions, there are others which do not conform to these, and all that one can do is to describe these ill-defined lesions as faithfully as one can. We have described a lesion of this type, and we must wait for more knowledge, so that a definite classification can be made.

SUMMARY

A case of reticulosis of the skin is described. The histologic similarity of the conditions grouped under the term lymphoblastomata is pointed out, and their origin is discussed, with the conclusion that they appear to arise from a stimulus acting on the primitive reticular syncytium.

OLIGOSEPSIS

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The term virulence indicates the degree of ability of pathogenic micro-organisms to produce infection. As experience has shown, this ability of a micro-organism to produce infection is not always the same in the end, and every pathogenic germ may be extremely virulent at times, while at other times it may exist as an entirely harmless parasite. Micro-organisms are extremely virulent as a rule after they have been transferred from one infected host where they have been able to produce a disease. However, when these germs are kept for a long time in artificial mediums, a gradual decrease of the virulence takes place, and their eagerness to fight is then slight. Virulent micro-organisms can be killed easily in vitro by any one of a number of chemical preparations. There is no proof as yet that it is possible to kill the germs by injecting antiseptic solutions into the living host. It is possible to protect the body against additional infection by asepsis, but the actual infection cannot be influenced in this way. It is not possible to decrease the actual infection either by antisepsis or by sepsis. I shall endeavor in this article to show that it is apparently possible to treat septic conditions by oligosepsis. The term "oligosepsis" indicates a chemotherapy directed against the virulence of pathogenic micro-organisms with the aim of reducing their infectious ability without necessarily killing them. In a paper on the chemistry of virulence published by me in 1934,[1] I tried to demonstrate that it is possible to decrease the virulence of pathogenic micro-organisms by chemotherapy in instances of actual infection.

Much[2] has shown that harmless parasitic, pathogenic micro-organisms can be made extremely virulent. Bacillus mycoides under natural conditions is an entirely harmless parasite. Mice inoculated with it have shown no pathogenic effects whatever. However, when Much inoculated mice with this harmless parasite and administered at the same time a solution of lactic acid, a most virulent infection resulted, and the mice died in from two to four days. Autopsy of these mice

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From the Longview Hospital.

1. Hallay, L.: Beitrag zur Chemie der Virulenz: Seifenschaumbehandlung von Hautentzündungen, Wien. med. Wchnschr. **84**:1254 (Nov. 10) 1934.

2. Much, H.: Chemie der Virulenz, Deutsche med. Wchnschr. **47**:321, 1921.

revealed immense quantities of bacilli crowded within the blood and internal organs. The same results were obtained by Much under normal conditions with a similarly harmless organism, Bacillus proteus X19, O and H. This artificial virulence was produced by 1 per cent and even 0.1 per cent solutions of lactic acid. Similar experiences with pathogenic germs have been reported previously by Behring.[3]

The fact that mass starvation, as observed on several occasions in the history of man, has been associated as a rule with epidemics of infectious diseases might be explained in the same way. It is known that starvation causes acidosis, and the acidosis apparently tends to increase the virulence of pathogenic germs and to make harmless parasites extremely virulent. The mass starvation caused by drought in Russia in 1891 was followed by a malignant epidemic of cholera. The starvation of the population in Poland during the Great War was associated with an epidemic of typhoid fever, typhus and dysentery. In the same country a case of typhus fever was a rare occurrence before the war, and as soon as the food supply of the Polish population improved after the war typhus virtually disappeared. It is doubtful that Rickettsia Prowazeki, which was considered responsible for the morbus typhus, was created in Poland during the war. Cowdry observed forty different types of this micro-organism in the alimentary canals of insects and arachnids, and no one of them under normal conditions has shown the tendency to produce typhus fever. A great percentage of the Polish population lives under the most unhygienic conditions; there is an enormous quantity of filth, and no one would be able to estimate the number of lice that populate a majority of Poland's poverty-striken population. Neither the unhygienic conditions nor the lice accordingly can be made responsible for the temporary malignant character of R. Prowazeki observed during the war. Apparently it can be explained only by the acidosis caused by mass starvation of the Polish population resulting from the terrible economic conditions during and after the war. This acidosis seems to have caused an extreme degree of malignancy in cases of infestation with R. Prowazeki, which was followed by many deaths due to typhus fever. Accordingly, either local acidosis or a general tendency to acidosis may increase the virulence of micro-organisms.

According to Schade, Neukirch and others, a local increase of the hydrogen ion concentration occurs in every inflammation. As Grothe showed, this local acidosis causes a destruction of tissue which is followed by an increase of the local acidosis. It appears reasonable that a vicious circle may develop. As Goldscheider stated, a vicious circle can be observed in almost all diseases and does not correspond with the

3. Behring: Centralbl. f. klin. Med. **9**:37, 1888.

notion of entelechy revived by the neovitalists in biology and in medicine. The vicious circle in inflammation, especially in inflammation caused by infection, does not appear to be purposeful, especially in cases in which this vicious circle causes the death of the infected person. Death in these cases appears to be due to the increased virulence of the micro-organism, which was caused by the avalanche-like development of the acidotic tendency.

The concentration of hydrogen ions in blood and in tissues is constant in a living organism. There are several biologic mechanisms which can be made responsible for the stability of this equilibrium. An important one depends on contraction of the capillaries in some of the tissues. Owing to this the quantity of blood circulating through these tissues is reduced, and an insufficient supply of oxygen results. According to Liebig, Pasteur and Warburg, inner respiration is then no longer possible, and fermentation replaces it. Owing to the want of oxygen, the dextrose cannot be resolved into carbon dioxide and water and the disintegration of the dextrose remains at the stage of lactic acid. One molecule of dextrose divides into two molecules of lactic acid. However, the least possible increase of the hydrogen ion concentration causes, according to Atzler, dilatation of the capillaries, which results in an improvement of the oxygen supply, and under normal conditions the lactic acid is oxidized into carbon dioxide and water. Accordingly, the mobile balance of the hydrogen ion concentration governs the mobile balance of the capillaries, and vice versa. The process develops as a unity of opposites. This balance suffers apparent disturbance in acute inflammations, and the tendency to balance seems to be disturbed in general septicemia.

Contrary to the views of Sauerbruch, who expressed the belief that local acidosis in inflammation is purposeful, and of Bálint, who tried to produce an alkalosis by administering alkaline solutions, it appeared reasonable to me that neither acidosis nor alkalosis was good for the treatment of inflammation. Theoretically reasoning seemed to suggest that the inflammation could be reduced and the virulence of the micro-organisms decreased by local or general restoration of the normal balance of the hydrogen ions by buffers.

The oldest experiences in treatment of inflammation with remedies which seem to be buffers are published in The Papyrus Ebers,[4] which is considered to be the oldest written document in medicine. According to The Papyrus Ebers, a "crocodile bite" had to be treated by covering it with raw meat the first day; "to draw out a splint of the flesh" application of "male and female semen" was advised; an "uases

4. Bryan, Cyril P.: Papyrus Ebers, New York, D. Appleton and Company, 1931.

abscess" had to be anointed with blood of a duck, a swallow and a goose; a prescription against a strong ulcer called for eggs of an ostrich for outer application; for the regulation of urine, "xet-plant" with milk had to be applied on the phallus, and for diseases of the tongue one was advised to "take milk and gargle with it." Raw meat, sperm, blood, egg and milk may be considered buffer substances because they are all proteins, and it is known that proteins, owing to their ambivalence, act as buffers in retaining the acid base balance. In the "Talmud" Rabbi Meyer advised milk for treatment of sore eyes. The "Leechbok of the Fifteenth Century" recommended for the treatment of sore eyes "milk of a mother who has borne a son," or cheese or white of an egg. This advice is followed by a statement that the remedy acts at once. Negroes in Kentucky used to treat gonorrheal ophthalmoblennorrhea by outer application of mother's milk. In various countries raw meat is a folk remedy for the treatment of wounds. Milk preparations are produced at the present time by two different companies in Europe. They have been used for a number of years with success.

In a paper published in April 1931 [5] I reported favorable results obtained by powdering the infected surface in erysipelas with sodium bicarbonate. It was possible in every case to stop the infection at once.

In a paper published in October 1931 Druen [6] reported on an epidemic of erysipelas in the state hospital for the insane at Allenberg, Germany. The epidemic was malignant; the first two patients who contracted the disease died in two days. The other twelve patients who acquired it afterward were treated by the *"Hallaysche Behandlungsweise,"* the affected part being powdered with sodium bicarbonate. Druen reported that all subjective symptoms disappeared at once and that all the patients recovered in from two to five days. It was possible to stop the epidemic in this way. In November 1931 Baumeister [7] reported a case of erysipelas in an old man who, in spite of energetic treatment, had a septic condition and was moribund. When powdered sodium bicarbonate was applied the patient recovered. I believe that this "specific" action of sodium bicarbonate in erysipelas has the following explanation: When sodium bicarbonate is applied to the dry skin as a powder it is not ionized and accordingly is not able to act as an alkali. However, this powdered dry sodium bicarbonate becomes ionized and acts as an alkali when acids appear in the powdered surface, the ionization occurring only to such an extent as to neutralize these acids. It appears reasonable that in this way application to the dry skin reproduces the buffer action of the sodium bicarbonate in the body artificially.

5. Hallay, L.: München. med. Wchnschr. **78**:674 (April 17) 1931.
6. Druen, A.: Psychiat.-neurol. Wchnschr. **33**:507 (Oct. 17) 1931.
7. Baumeister, H.: Psychiat.-neurol. Wchnschr. **33**:567 (Nov. 21) 1931.

In an article published in September 1931 [8] I tried to demonstrate another mechanism for restoring the acid-base equilibrium in infection. My own experiences, in accordance with the older empiricism, have shown that almost all processes of inflammatory infection in the body may be influenced favorably by hydrotherapeutic sweating procedures. Contrary to Marchionini's belief that this favorable action of the sweating is due to the "purposeful" mantle of acid sweat which appears during the treatment, I tried to show that this favorable action of the sweat is apparently due to the loss of acid by the increased perspiration and to the increased oxidation of the acids caused by the active hyperemia.

In two papers, published in 1932 [9] and in 1934,[10] respectively, I tried to show that septicemic processes, according to my own experiences and according to the empirical practice of centuries in official and in folk medicine, can be influenced favorably by an antiketogenic diet (a diet rich in sugar content).

In a paper published in October 1934 [1] I was able to report favorable results obtained by the oligoseptic treatment of infections of the skin with soap lather. Like powdered sodium bicarbonate, soap lather seems to be a buffer. The degree of ionization of soap lather, especially when the lather is dried in and covers the skin as a thin layer, is practically null. The infected portion of the skin and the area immediately surrounding it were lathered, and the lather was allowed to dry in. Afterward a thin layer of soap appeared. The contact of the cold soap with the inflamed skin caused an instantaneous disappearance of the pain (analgesic action of alkali was reported by Gaza and Brandi in 1918). The tension, the redness and the swelling decreased gradually afterward and in some instances disappeared entirely in about twelve hours. Beginning abscesses become absorbed. An incision could not be avoided, however, when the destruction of tissue had developed considerably.

Powdered sodium bicarbonate and soap lather can be employed as buffers only on the uninjured, intact and dry surface of the skin. When those substances are employed on a wounded surface or on a moist mucous membrane, no buffer action can be obtained. In these cases both sodium bicarbonate and soap act as alkalis and cause irritation and destruction of tissue. A local buffer action may be obtained on infected mucous membranes by protein preparations, according to experiences which may be traced back to almost 4000 B. C.

These experiences, which are based on purely empirical observations, and my own experiences, as published in the papers mentioned, give

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8. Hallay, L.: Med. Welt **5**:1352 (Sept. 19) 1931.
9. Hallay, L.: Biol. Heilkunst **13**:221 (April 2) 1932.
10. Hallay, L.: Naturärztl. Rundschau **6**:175 (June) 1934.

much evidence that the virulence of pathogenic micro-organisms may be reduced enough in actual infection by buffers to make the pathogenic micro-organisms apathogenic harmless parasites primarily and to get rid of them secondarily.

SUMMARY

Harmless parasites can be made extremely virulent by treatment with acids. The acidosis effected by the infection increases the virulence of pathogenic micro-organisms. In actual infection, pathogenic micro-organisms can be made harmless by restoring the acid-base balance in the infected area. This is apparently possible: by (1) hydrotherapeutic procedures designed to produce sweating; (2) by antiketogenic diet; (3) application of powdered sodium bicarbonate or of soap lather as buffers in infections of the skin; (4) application of protein buffers in infections of mucous membranes. The oligosepsis produced in this way is apparently the most harmless and the most proficient way of treating acute infections.

PENOSCROTAL ELEPHANTIASIS OF LYMPHO-GRANULOMATOUS ORIGIN

DESCRIPTION OF A CASE WITH PSORIASIFORM CUTANEOUS LESIONS AND OTHERS RESEMBLING AN ECTHYMATOUS PYODERMA

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AND
HERMES AHUMADA, M.D.
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Lymphotropism of the virus of Nicolas-Favre's disease is an undisputed fact; neurotropism and dermotropism have only recently been considered as possible. Local cutaneous lesions distinctly lymphogranulomatous in nature have been described by Nicolas and Favre, Massia and Lebeuf, Chevallier and Bernard, Pinard and Fiehrer, and Sézary. Howard and Strauss [1] found anal condylomas in a man and regarded them as an unusual manifestation of the disease.

Two types of general cutaneous lesion have been described in lymphogranuloma venereum (inguinale), one resembling erythema multiforme and the other erythema nodosum.

Koppel [2] reported three cases of the inguinal syndrome accompanied by erythema nodosum; Hellerstroem [3] described similar cutaneous lesions in four such cases; Buschke referred to one case in which the condition was accompanied by an exanthem; Kleeberg [4] and Kerl reported metastatic cutaneous symptoms resembling erythema nodosum in addition to inguinal adenopathy in lymphogranuloma venereum; Nicolau [5] described the case of a woman suffering from vulvo-anorectal elephantiasis, who had cutaneous lesions on the buttocks and on the right labium majus. These consisted of rectangular squamous plaques strewn with small nodules. The presence of the virus of lymphogranuloma venereum in the skin over the diseased glands has been demonstrated by Franchi,[6] who expressed the belief that when it is present it is transmitted from

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From the Urological Clinic of Prof. J. L. Bisquertt, Clinical Hospital, Medical College, Chile University.

1. Howard, M. E., and Strauss, M. J.: New England J. Med. **212**:323 (Feb. 21) 1935.
2. Koppel, A.: Klin. Wchnschr. **6**:2469, 1927.
3. Hellerstroem, S.: Acta dermat. venereol., supp. 1, 1929, p. 130.
4. Kleeberg, L.: Dermat. Wchnschr. **91**:1376 (Sept. 13) 1930.
5. Nicolau, S.: Ann. de dermat. et syph. **5**:1, 1934.
6. Franchi, F.: Bull. Soc. franç. de dermat. et syph. **41**:165, 1934.

the glands by contiguity; lately Pisacane [7] in two of five cases found that the skin was involved and that the localization of the process was particularly perivascular and mesenchymal.

In 1934 Franchi [6] found that the fluid from the cutaneous exanthem that occasionally develops in the course of the disease gives a positive Frei reaction; the same year Midana [8] described a case of lymphogranuloma venereum in which there were superimposed adenopathy and cutaneous lesions of the gluteal regions, abdomen and thighs which looked like an ordinary pyoderma of the ecthymatous type. An extract from these lesions produced an intensely positive Frei reaction in the patient himself and in others suffering from lymphogranuloma venereum and a negative reaction in healthy controls. Autoinoculation of the patient's skin with material from the lesions produced changes of the same kind as in the Frei test. This proved the specific nature of the cutaneous lesions, as well as of the enlargement of the lymph nodes.

The case which we shall describe is one of an unusual lymphogranulomatous syndrome. Only a few such cases have been reported so far (Barthels and Biberstein,[9] Coutts and his associates,[10] Santapau [11] and Stryker and Ploch [12]).

REPORT OF CASE

L. A. V., a man aged 36, single, was admitted to the hospital on July 9, 1936. His family history was of no importance. He stated that he smoked and drank heavily and had enjoyed good health. Two years previously, through an accident, he had lost the sight of the right eye. A marked hoarseness had existed ever since his ninth year.

He gave a history of gonorrhea in 1927, with discharge for fifteen days, after which there were no further symptoms or complications. He did not submit to any treatment. A few months later in the same year a single chancre appeared in the balanopreputial region. This was diagnosed as syphilitic. The Wassermann reaction of the blood was 2 plus at the time. He did not receive any treatment. In 1928, without his having noticed any open lesion on the genital organs, an adenopathy in the left inguinal region set in, accompanied by fever, cephalalgia and general malaise. Ten days later the affected glands opened spontaneously, and fluid pus was evacuated freely. A fortnight afterward all symptoms had disappeared. In 1930 several perigenital erosions made their appearance, and notwith-

7. Pisacane, C.: Arch. ital. di dermat., sif. **11**:66, 1935.

8. Midana, A.: Gior. ital di dermat. e sif. **75**:1743, 1934.

9. Barthels, C., and Biberstein, H.: Beitr. z. klin. Chir. **152**:325, 1931.

10. Coutts, W. E., and Banderas Bianchi, T.: Urol. & Cutan. Rev. **38**:263, 1934. Coutts, W. E., and Martini Herrera, J.: Dermat. Wchnschr. **98**:784 (June 23) 1934.

11. Santapau, O.: Med. mod. **7**:248, 1934.

12. Stryker, G. V., and Ploch, B.: Elephantiasis of the Penis and Scrotum: Sequela of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **32**:86 (July) 1935.

standing a negative Wassermann reaction the attending physician ordered antisyphilitic treatment. Neoarsphenamine was administered in one dose of 0.15 Gm. and three of 0.3 Gm. As the lesions disappeared, the patient abandoned all treatment.

The inception of the present illness had been noted one year before, when a slight urethral discharge appeared. This subsided without any treatment. At about that time the patient noticed that his genital organs began gradually to increase in size. This asymptomatic swelling continued and by the end of six months was considerable. At the end of that period squamous cutaneous lesions made their appearance on both legs and gluteal regions. Those changes in the skin increased gradually and invaded neighboring tissues, developing into large

Front and side views of patient, showing enlargement of genitalia.

plaques. Pruritus and secretion had appeared in the last two months at the level of these patches. The genital organs continued to enlarge.

In general appearance the patient seemed healthy. The heart and the lungs were normal. The external genitals were considerably increased in size. A hard edematous infiltration of the skin of the scrotum and penis reached over the suprapubic zone. The gonads could not be felt distinctly through this swelling. There was a scar in the left inguinal region. No discharge came from the urethra. The urine was clear and without threads. The prostate was slightly enlarged transversely and of harder consistency than normal. There were extensive cutaneous lesions in the lower extremities and the gluteal regions. These were partly squamous. Ulcerations of an ecthymatous appearance were present in certain zones of these plaques.

Laboratory tests gave positive Wassermann and lymph[13] reactions and a 4 plus Kahn reaction. Results of the Frei intradermal test were negative.

13. Coutts, W. E., and Ponce, T.: J. Lab. & Clin. Med. **20**:629, 1935.

Examination of the eyeground (left eye) by Dr. Borgoño showed marked peripapillary edema, dilatation and tortuosity of the veins and intensely dark coloration of the circulating blood. The eyegrounds were lymphogranulomatous.

The pressure of the spinal fluid was normal. The content of albumin was 0.15 Gm. and of chlorides 7.2 Gm. per hundred cubic centimeters. Red blood corpuscles were numerous. Wassermann, Nonne-Apelt and lymph reactions were negative. There was a positive Pandy reaction.

Urinalysis showed a specific gravity of 1.012 and a content of chlorides of 11.5 Gm. and of urea of 10.24 Gm. per hundred cubic centimeters. Bacteria were also present. The urea content of the blood was 0.23 Gm. and the sugar content, 0.60 Gm. per hundred cubic centimeters. The blood count showed 4,840,000 red corpuscles and 9,600 white corpuscles per cubic millimeter. The basal metabolism was 45.2 calories per square meter per hour (nominal 39.5), or 14.4 per cent above normal. The respiratory quotient was 0.78.

Histologic examination by Prof. E. Croizet of a specimen from the scrotum disclosed a diffuse edematous condition of all the sample, slight hyperplasia of the malpighian epithelium of revestment and lymphoplasmocytic infiltration of the scrotal dermis. Fibrosis of its deeper portions extended among the muscle fibers of the dartos, producing their dissociation. In the dartos islets of nodular lymphocytes were found frequently.

An antigen was prepared from the cutaneous lesions according to routine technic and tested for sterility of aerobes and anaerobes. Utilized in patients suffering from lymphogranulomatous syndromes, this proved active but in healthy controls gave negative results.

RHINOSCLEROMA

REPORT OF A CASE

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I have reported two cases of rhinoscleroma in California previously,[1] and Bingham and Cutler [2] described a third. So far as I know, these are the only cases to have been reported in this state, although there may be many more undiscovered cases in this part of the country, for lesions are seen occasionally in the mouth only. It is possible that among the Mexican and Central American population there may be many "carriers." The subject of the present report lives in a district of the San Joaquin valley where there are many laborers from Mexico and Central America, but she stated that she had never seen any one with lesions like hers or like those in my collection of photographs. She was presented at a meeting of the San Francisco Dermatological Association in April 1936.

REPORT OF CASE

Mrs. B., an American housewife aged 29, was referred by Dr. O. P. Diederich of Fresno in 1934. She presented an enormous nodular growth on the nose, the upper lip and the hard palate, as shown in figures 1 and 2. The left nostril was almost completely obstructed. There were palpable glands in the submaxillary and anterior cervical regions. The first lesions, those on the hard palate, were seen in 1921, the lesions on the lips and nostrils in 1927 and the external nasal growth in 1930. It is possible, of course, that small intranasal lesions were present and unnoticed before the palatal growth was discovered.

The patient lived as a child in Arkansas and Oklahoma, but since she was 12 years old she has resided in the San Joaquin valley, where there are many Mexican laborers.

Her personal and her family history are irrelevant. She has three healthy young children. She is rather obese and in apparently excellent health, except for her rhinoscleroma.

Repeated blood counts, urinalyses, Wassermann examinations of the blood, analyses of stools and gastric contents, roentgen examinations of the gastro-intes-

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1. Alderson, H. E.: Rhinoscleroma: Progress Notes on a Case Previously Reported, J. Cutan. Dis. **34**:198 (March) 1916; A Case of Rhinoscleroma, ibid. **32**:308 (April) 1914; Scleroma: Report of a Case, Arch. Dermat. & Syph. **26**: 639 (Oct.) 1932.

2. Bingham, E. M., and Cutler, O. I.: Rhinoscleroma, California & West. Med. **42**:463 (June) 1935.

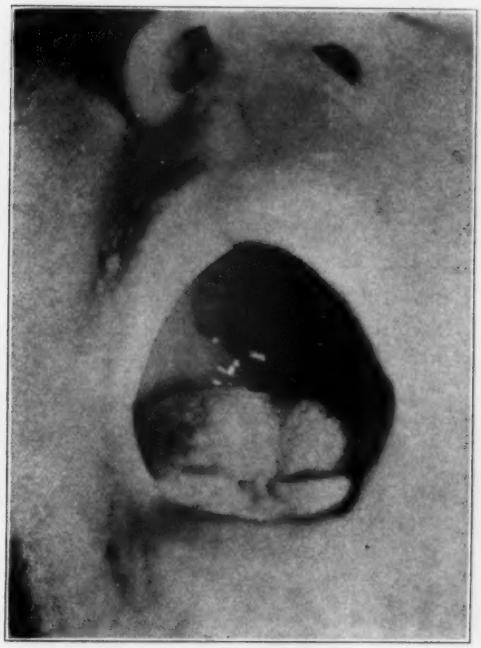

Fig. 1.—Nodular lesions characteristic of rhinoscleroma appear on the palate.

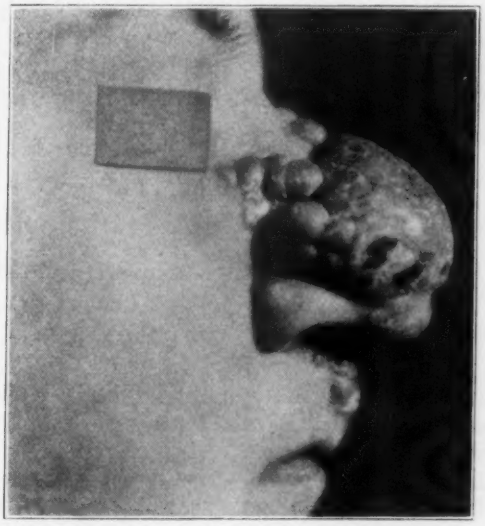

Fig. 2.—Appearance of lesion on the nose.

tinal tract and attempts to visualize the gallbladder all gave negative results. The patent's basal metabolic rate was —8 per cent.

In March, June and November 1934 she was given heavy low voltage and high voltage roentgen therapy. This was repeated in May 1935, at which time the roentgenologist gave her nupercaine ointment in an attempt to modify an expected reaction to the roentgen rays. The application was followed by violent inflammation, with much edema extending over the "flush area" of each cheek. After this acute inflammation subsided, extensive nodular areas of rhinoscleroma remained, involving most of both cheeks. All of the areas persisted as they were in 1935,

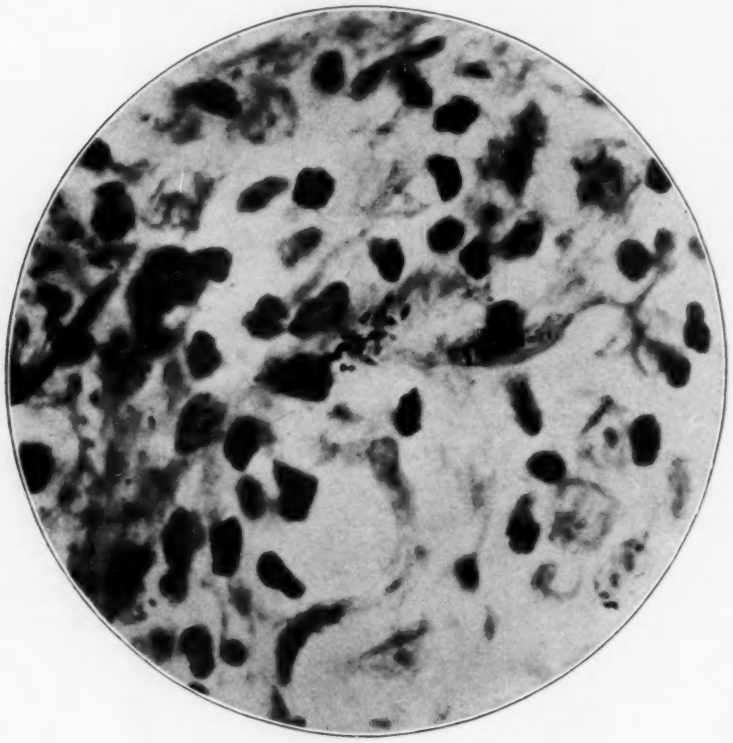

Fig. 3.—Section showing Mikulicz cells containing Frisch bacilli.

except that the nose was much smaller and the lesions of the cheek flattened considerably.

Repeated attempts to grow the organism have been unsuccessful, but Frisch bacilli were readily demonstrated in stained sections. Sections were stained for acid-fast organisms, but none were found.

Dr. Arne Ingels reported the results of his studies of the sections as follows:

"The epidermis shows thinning (in places only two or three layers of cells remain). No hyperkeratosis or parakeratosis is present. Moderate intercellular and intracellular edema is seen. The regular arrangement of the epithelial cells, including the basal cell layer, is maintained. Sections stained for melanin (Becker stain) show absence of pigment in the basal cell layer.

"The rete pegs are almost completely obliterated. A narrow zone corresponding to the papillary layer is comparatively free from inflammatory changes. Otherwise the cutis shows dense masses of infiltration with round cells, consisting mainly of lymphocytes. A few mast cells and histiocytes are seen. Some large areas show a lighter appearance, due to the frequency of Mikulicz cells. Sections treated with the Gram stain show many gram-positive cocci and rod-shaped encapsulated Frisch bacilli, both in the Mikulicz cells and extracellularly. Giant cells of the foreign body type are seen in the vicinity of the foam cells, whereas no areas of caseation or tubercles are present.

"Staining for acid-fast bacilli gave negative results. The abundance of sebaceous glands in the sections is explained by the site from which the biopsy material was removed, i. e., the vicinity of the nose. The diagnosis is rhinoscleroma."

In 1935 Bingham and Cutler reported a case of the disease in a Mexican in Riverside, Calif. This case and my three examples constitute, as far as I know, the only cases in California that have been reported.

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DEMONSTRATION OF PEMPHIGUS TOXIN IN FRESH AND IN DRY BLOOD

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INTRODUCTION

In previous papers I have described the results of the phytopharmacologic examination of various body fluids, toxins and chemicals and have pointed out that blood, blood serum and blood plasma from normal subjects exhibit a slight toxicity for roots of Lupinus albus seedlings grown under carefully controlled plant-physiologic conditions.[1] Such seedlings, grown in solutions of blood serum and blood plasma from normal subjects (obtained with highly purified heparin), yielded a phytotoxic index of from 70 to 75 per cent, as compared with that of control seedlings grown in normal plant-physiologic solution alone. Lupinus seedlings grown in whole blood, either laked or kept fluid with heparin, gave phytotoxic indexes ranging from 65 to 70 per cent. When similar methods were applied to the study of specimens of blood from patients with various diseases, it was found that specimens of serum from patients with most pathologic conditions exhibited little or no variation in toxicity from those of normal subjects, but that specimens from patients with certain diseases showed a definite increase. By means of the phytopharmacologic test it was discovered that the blood serum, blood plasma, whole blood and various secretions (sweat, tears, milk, etc.) of menstruating women, particularly at the beginning of catamenia, possessed a marked toxicity.[2] Thus the presence of a toxin (called menotoxin) in such fluids was established. It was even more interesting to find that Lupinus seedlings grown in solutions of blood serum from patients with true pernicious or Addison's anemia also exhibited

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From the Pharmacological Research Laboratory, Hynson, Westcott & Dunning, Inc.

1. Macht, D. I., and Livingston, M. B.: Effect of Cocaine on the Growth of Lupinus Albus: A Contribution to the Comparative Pharmacology of Animal and Plant Protoplasm, J. Gen. Physiol. **4**:573-584, 1922.

2. Macht, D. I., and Lubin, D. L.: A Phytopharmacological Study of Menstrual Toxin, J. Pharmacol. & Exper. Therap. **22**:413-466, 1924. Macht, D. I., and Davis, M. E.: Experimental Studies, Old and New, on Menstrual Toxin, J. Comp. Psychol. **18**:113-134, 1934.

a toxic reaction.[3] Specimens of serum from patients with this disease yielded phytotoxic indexes of not more than 55 per cent and often as low as 40 per cent. This finding marked the first experimental demonstration of the presence of a toxic substance in the blood of patients with pernicious anemia. Furthermore, the phytopharmacologic test has since proved a valuable means of differentiating that disease from secondary anemia, leukemia, Hodgkin's disease and other pathologic conditions of the blood, specimens of serum from which do not yield such low phytotoxic readings. It has also been employed to gage the relative values of various therapeutic measures employed in treating patients with pernicious anemia.[4]

The most extensive phytopharmacologic study of specimens of blood from diseased patients was carried out by me in collaboration with the dermatologist Dr. Isaac R. Pels. We undertook a systemic study of blood serum from patients with all kinds of cutaneous diseases and found that in the vast majority of dermatoses the serologic specimens were not more toxic for plant protoplasm than were specimens from normal human beings. The serum from patients with pemphigus, however, constituted a striking exception. Specimens from numerous patients with pemphigus gave indexes of 58 or 59 per cent, as compared with readings of from 70 to 75 per cent for those from normal patients. Specimens from patients with erythema multiforme and other diseases simulating it gave normal readings. The same was true of specimens obtained from patients with dermatitis herpetiformis and the Senear-Usher syndrome. Serum from patients with one other disease, leprosy, also revealed a marked toxicity for Lupinus seedlings.[5]

In pursuing such studies for diagnostic purposes, I usually employed the blood serum, because quantitative measurements could be made more conveniently with that fluid than with plasma or whole blood. Physicians usually collect the two latter with the aid of such anticoagulants as oxalates, citrates and fluorides, all of which are poisonous for plants and would therefore interfere with the phytopharmacologic test. The

3. Macht, D. I.: A Phytopharmacological Study of Pernicious Anemia, J. Pharmacol. & Exper. Therap. **29**:461-469, 1926; Pernicious Anemia: An Experimental Contribution to the Etiology, Diagnosis and Treatment, J. A. M. A. **89**: 753-759 (Sept. 3) 1927; Studien über das Gift der perniziösen Anämie, Arch. f. exper. Path. u. Pharmakol. **123**:290-304, 1927.

4. Macht, D. I., and Anderson, W. T.: Clinical and Experimental Studies on Phototherapy in Pernicious Anemia, J. Pharmacol. & Exper. Therap. **34**:365-389, 1928. Macht, D. I.: Treatment of Pernicious Anemia by Ultraviolet Rays, Brit. J. Actinotherapy **5**:228-231, 1931.

5. Macht, D. I.: Phytopharmacological and Photopharmacological Studies on Leprosy Blood Serum, J. Philippine Islands M. A. **8**:523-524, 1928; Phytopharmacological Studies on the Sera of Pemphigus, Syphilis and Leprosy, Acta dermat. **18**:126-138, 1932.

only anticoagulant that is not toxic for plants is highly purified heparin, which will be discussed in a succeeding paragraph. Dr. Pels and I have studied more than two thousand specimens of blood serum for the purpose either of establishing a diagnosis of pemphigus or of differentiating that disease from pathologic conditions simulating it. It was found that in the great majority of cases the phytopharmacologic diagnoses agreed with the clinical diagnoses made when the specimens were taken or those established by the later course of the disease. No specimens forwarded to my laboratory for examination, however, had any distinguishing mark but a number, so that I did not know the condition of the subject from which it came or even whether he was normal or diseased. Later, when the phytopharmacologic findings and clinical diagnoses were compared, it was found that they were in striking agreement.

Dr. Pels and I have described the phytopharmacologic test in a number of prior publications.[6] However, since certain workers have had difficulty in mastering the technic and have obtained inconsistent results, I consider it opportune to preface a discussion of hitherto unpublished data and newly discovered phenomena with a more detailed description of the method than I have yet presented.

EXAMINATION OF FRESH BLOOD FROM PATIENTS WITH PEMPHIGUS

Fresh blood serum is almost invariably employed in making this test. Occasionally serum from the bullae is also examined. A 1 per cent solution is prepared by dissolving the serum in equal parts of distilled water and Shive's plant-physiologic solution,[7] which consists of 10.4 cc. of a 0.5 molar solution of chemically pure calcium nitrate, 30 cc. of a 0.5 molar solution of chemically pure magnesium sulfate and 36 cc. of a 0.5 molar solution of diacid potassium phosphate (KH_2PO_4), to which is added enough distilled water to make 1 liter. In testing body fluids for clinical purposes it is absolutely necessary to use salts of the highest chemical purity. Even the test tubes employed in such work should be of a special type, i. e., they should be made of hard or nonalkaline glass, in order that all conditions of experimenta-

6. Macht, D. I., and Pels, I. R.: Demonstration of Toxin in Cases of Pemphigus, Proc. Soc. Exper. Biol. & Med. **25**:237-238, 1927. Pels, I. R., and Macht, D. I.: Phytopharmacologic Examination of the Blood in Pemphigus and in Some Other Diseases of the Skin, Arch. Dermat. & Syph. **19**:640-647 (April) 1929; Phytopharmacology of Pemphigus and Other Dermatoses: Additional Studies, ibid. **23**:601-603 (April) 1931.

7. Shive, J. W.: A Study of Physiological Balance in Nutrient Media, Physiol. Researches **1**:327-397, 1915.

tion may be rigidly controlled and standardized. The hydrogen ion concentration of a mixture of equal parts of distilled water and Shive's solution is usually about 5. When blood serum is added to make a 1 per cent solution, the p_H shifts toward the alkaline side and varies from 5.4 to 5.6. I have shown in prior publications that such slight variations in p_H have little effect on the growth of seedlings immersed in the solutions and are certainly not sufficient to account for differences in toxicity between specimens of serum from normal and from diseased subjects. As a matter of fact, there is usually no difference at all in hydrogen ion concentration between a 1 per cent solution of serum from a normal subject and a like solution from a diseased subject.

In making the phytopharmacologic test, I employ a special apparatus containing twenty-three parallel rows of ten perforations for holding test tubes in an upright position. The ten tubes in the first row, and sometimes those in two or three such rows, are filled with control solutions consisting of equal parts of Shive's saline solution and distilled water. Succeeding rows of ten tubes each are filled with 1 per cent solutions of various specimens of blood serum to be dissolved and tested in the plant-physiologic saline solution. The Lupinus albus seedlings are then carefully selected, measured and immersed in the solutions filling the upright tubes. For ordinary routine examinations an average of ten seedlings for each solution to be tested is usually sufficient for a single experiment. The test should be repeated on several consecutive days, however, until the phytotoxic indexes differ from each other by no more than 5 per cent. Such repetition of the test, on two days at least, is necessary, because occasional crops of Lupinus albus yield seedlings impervious to saline solutions of toxins. Such seedlings give a negative reading or an index considerably higher than that yielded by controls in normal blood serum. While it is true that specimens of serum obtained from patients with certain rare conditions (i.e., virus diseases, etc.) consistently give higher readings,[8] such conclusions can be deduced only from several tests. In dealing with specimens of serum of patients suspected of having pemphigus, pernicious anemia or some similar condition, negative or exceedingly high readings after a single examination should be regarded as "no takes" if in several successive repetitions of the test toxic effects are definitely exhibited.

The seeds which I employed in my phytopharmacologic studies are those of Lupinus albus, the large variety. Such seeds should not be old or worm eaten, although those which are one or two years old are satisfactory. A quantity of the Lupinus seeds is soaked overnight in water from the tap. The following day the swollen seeds are ready for

8. Macht, D. I., and Gardner, R.: Phytopharmacological Reactions of Normal, Toxic and Atoxic Sera, Proc. Nat. Acad. Sc. **22**:384-389, 1936.

planting. Finely ground sphagnum was found to be the most suitable medium for the problem in hand. The sphagnum should not only be ground to a fine powder but should also be impregnated with just the amount of water most suitable for optimum germination. Here the beginner in phytopharmacology encounters his first difficulty. If the moss contains too much moisture, the seeds will rot, fungi will develop, germination will be defective and the seedlings will be diseased. If it contains too little water, the seedlings will suffer from malnutrition and lack of turgor and will exhibit a stunted growth. A great deal of experimentation has proved that the best results are obtained with sphagnum containing from 70 to 80 per cent of water by weight. Such a medium can be successfully prepared only after considerable practice. Sphagnum prepared for the germination of seedlings must usually be rinsed several times with hot water to free it from an excess of acid matter, which would interfere with proper development of the plants. It must also be well aerated before it is deposited in the glass jars in which the seeds are to be planted. Swollen seeds, which have been soaked overnight, are planted closely together with the hili pointing down. In this way a large number of seedlings can be raised in a comparatively small area. A light layer of the moss is then sifted over the seeds, and the covered jar is allowed to stand in the dark for several days at room temperature. When the weather is mild, the seedlings are generally of convenient length for testing on the third day after planting. In winter, however, germination progresses more slowly even at room temperature, and the seedlings are not long enough until the fourth day after planting.

The most suitable seedlings for the phytopharmacologic test are those with roots measuring from 35 to 50 mm. Shorter seedlings may be employed, but their growth is usually not so rapid as that of the longer ones. For this reason in recent years I have been discarding those less than 30 mm. long. On the other hand, much longer seedlings exhibit curvatures which make them difficult to measure. Healthy seedlings are taken out of the moss; the adhering particles are removed by gentle brushing or rinsing, and the length of their roots is measured with a millimeter rule. Here the beginner encounters a second difficulty. While the line of demarcation between root and stem is usually definite and easy to find with the naked eye, with or without the aid of some innocuous staining solution, consistently accurate readings can be made only after much practice and experience. After the seedling has been measured, it is immersed in a tube of either the control solution or the blood serum solution to be examined. In this way ten seedlings are selected for each solution tested, including controls. The roots of the seedlings in any given experiment must be measured both at the beginning and at the end of the test by the same person. A woman

experimenter should not handle the plants at the time of catamenia. All experimenters should wash their hands carefully before touching the objects to be tested.

An important detail of technic is the matching of seedlings, i. e., the selection of seedlings of as nearly the same length as possible. Experiments with living plants are generally more reliable than those with living animals because of the vastly larger number of the former available and the physical and economic obstacles to such wholesale experimentation with higher animals. To insure maximum accuracy in performing the phytopharmacologic test, however, the seedlings selected should be of as nearly the same length as possible. Especially should the individual plants in corresponding positions in different rows be closely matched. This is accomplished by filling the first tubes of each row with seedlings of as nearly the same length as possible and then filling the second tube in each row with similarly matched seedlings and matching in the same way all the plants in corresponding tubes in the remainder of the rows.

When such a procedure is followed, deviations in readings due to differences in growth between seedlings which are either too long or too short at the outset of the experiment are reduced to a minimum, and a more reliable comparison can be made with regard to the effect of various solutions on the growth of the roots.

After all the seedlings have been measured and allotted to their respective tubes, the outfit containing them is placed in a refrigerator or a low temperature incubator. The seedlings are allowed to grow there in the dark for twenty-four hours, at the end of which time they are measured again, and the average increment of growth in control and unknown solutions is determined. The average growth of roots in any given solution of blood serums divided by the average increment in the length of roots of control seedlings grown in Shive's solution alone and maintained under exactly the same conditions—light, temperature, etc.—gives the so-called phytotoxic index of growth for that serum. Thus blood from normal subjects yields a phytotoxic index ranging from 70 to 75 per cent and serum from patients with pemphigus, a reading of 58 or 59 per cent.

Perhaps the most important single factor affecting phytopharmacologic testing of serum from patients with pemphigus is the temperature. It is absolutely necessary that seedlings grown in various solutions of serum be maintained at the temperature most suitable for the test. In earlier publications I specified 20 C. as the temperature most suitable for such work. Later experience, however, has shown that the best results in testing specimens of serum from patients with pemphigus are obtained with seedlings grown at a considerably lower tempera-

ture. The blood from such patients changes rapidly when kept at room temperature. The pemphigus toxin decomposes even at from 18 to 20 C. in the presence of the slightly acid Shive solution. Furthermore, the stimulus to growth of seedlings kept at temperatures higher than 15 C. is so great that the slight inhibitions produced by the presence of small quantities of toxin are masked. On the other hand, when the seedlings are maintained at temperatures below 15 C. the growth of all, even those in normal control solutions, is greatly retarded; as a consequence, the phytotoxic indexes yielded by specimens of both toxic and normal blood are much lower than they should be. In other words, seedlings grown in solutions at temperatures lower than 15 C. give more toxic readings than those grown in similar solutions at 15 C. Of all the ecologic factors playing rôles in phytopharmacologic work with blood, temperature is the most important. Undoubtedly some investigators attempting the test have obtained discordant results because they did not regard this all-important ecologic factor. It is obvious, moreover, that all specimens of blood sent for phytopharmacologic testing, especially those from patients in whom pemphigus is suspected, should be protected from light and, preferably, kept on ice. I have repeatedly observed that the red blood corpuscles of blood affected by pemphigus undergo decomposition much more rapidly than normal erythrocytes and effect a purple hemolyzed fluid quite unsuitable for phytopharmacologic examination.

ILLUSTRATIVE EXAMPLE

To illustrate the findings obtained in phytopharmacologic testing of specimens of serum from normal and diseased patients, especially for careful research, the following description of a major experiment is given. In this instance seedlings grown in solutions of serum from normal human beings and in a mixture containing specimens of serum from several patients with pemphigus were compared with normal controls placed in Shive's solution. In routine diagnosis an average of ten seedlings is considered sufficient for a single experiment, and if the readings from two or three such tests, made on consecutive days, differ by no more than 5 per cent, the phytotoxic index is considered decisive. In this instance one hundred and twenty-five seedlings were grown simultaneously in each of three solutions, i. e., a normal Shive solution, a 1 per cent solution of blood serum from normal subjects and a 1 per cent solution of blood serum from subjects with pemphigus. All the seedlings had come from the same crop of Lupinus albus and were measured, matched, placed in their respective solutions, kept in the dark and incubated at a temperature of 15 C. for twenty-four hours, after which they were remeasured, and their phytotoxic indexes were calculated. Not only was the average growth under standard conditions

of each seedling determined, but a careful statistical study by modern mathematical methods was carried out in this connection. The standard deviation (S. D.) was determined by the well known formula, $\sigma = \sqrt{\frac{\Sigma D^2}{N}}$ and the probable error (P. E.) was established by this formula, P. E. (av.) $= \frac{.6745 \times \text{Standard Deviation}}{\sqrt{N}}$

TABLE 1.—*Experiment of Nov. 13, 1936*

(1) Growth in millimeters of each of 115 Lupinus albus seedlings in Shive's physiologic solution (controls); p_H, 5.1

16	17	20	15	16	13	20	19	19	15	18
15	13	15	15	11	16	17	15	19	16	21
12	16	17	17	17	16	16	20	14	16	19
17	14	17	15	18	15	15	15	19	13	17
14	14	13	16	17	19	14	19	13	18	19
20	13	15	19	13	14	14	12	14	17	
13	20	15	9	10	17	21	18	12	18	
15	17	16	15	11	20	19	19	10	20	
18	15	14	14	16	15	11	14	15	20	
15	18	16	13	18	15	9	13	9	10	
17	17	18	13	18	16	16	19	15	15	

Total growth of 115 roots, 1,810 mm.; average increment of each seedling, 15.74 mm.

S. D. (standard deviation) : $\sigma = \sqrt{\frac{\Sigma D^2}{N}} = 2.72$ mm. P. E. (probable error) : $\frac{0.6745\ \sigma}{\sqrt{N}} = 0.171$

(2) Growth in millimeters of each of 115 Lupinus albus seedlings in 1 per cent blood serum of normal subjects in Shive's solution; p_H 5.6

13	12	11	7	15	13	13	13	15	13	16
15	14	15	11	15	11	12	13	12	15	14
12	12	16	13	8	11	17	13	9	7	15
12	11	11	10	12	13	10	11	13	10	15
12	11	11	12	11	14	17	13	12	9	9
11	10	11	17	12	14	14	12	16	9	
13	10	14	13	13	13	12	14	15	15	
9	12	11	16	12	14	8	15	15	15	
11	11	13	15	13	10	15	11	8	12	
12	10	11	12	10	10	12	14	7	12	
14	12	12	11	10	15	13	11	11	14	

Total growth of 115 roots, 1,417 mm.; average increment, 12.32 mm.; phytotoxic index, 78%

S. D. (standard deviation) : $\sigma = \sqrt{\frac{\Sigma D^2}{N}} = 2.20$ mm. P. E. (probable error) : $\frac{0.6745\ \sigma}{\sqrt{N}} = 0.138$

(3) Growth in millimeters of each of 115 Lupinus albus seedlings in 1 per cent blood serum from patients with pemphigus in Shive's solution; p_H, 5.6

7	11	9	10	10	10	7	7	9	3	7
9	7	6	11	7	9	6	9	9	12	9
8	9	10	5	5	7	6	6	10	11	10
10	9	9	3	5	4	5	8	8	11	10
11	9	8	10	10	8	5	5	6	11	9
11	6	6	8	2	7	4	2	11	7	
11	6	5	4	7	6	9	5	9	3	
11	10	8	8	5	10	9	6	9	8	
7	6	7	8	10	5	8	7	8	3	
9	9	9	9	11	5	11	7	6	3	
10	8	6	11	3	6	10	11	7	8	

Total growth of 115 roots, 886 mm.; average increment, 7.704 mm.; phytotoxic index, 49%

S. D. (standard deviation) : $\sigma = \sqrt{\frac{\Sigma D^2}{N}} = 2.37$ mm. P. E. (probable error) : $\frac{0.6745\ \sigma}{\sqrt{N}} = 0.149$

The figures obtained in this major experiment are given in full. They reveal that the difference in growth between plants incubated in specimens of serum from normal subjects and from those suffering from pemphigus is so striking that it cannot possibly be due to chance or deviation in the individual measurements of various plants. This

experiment, in which the hydrogen ion concentration was also carefully followed, established conclusively not only the specific toxicity of serum from patients with pemphigus but also the reliability of the phytopharmacologic method—a method which certainly compares favorably with zoopharmacologic procedures, it being hardly conceivable that a comparison of three unknown solutions could be made on one hundred twenty-five higher animals simultaneously in an ordinary laboratory. Such an investigation could be conducted only in government laboratories or in a large research institution with a host of technicians, and even there it is doubtful if the findings obtained in a series of such tests with animals would show less deviation and error than those deduced by phytopharmacologic methods. The phytotoxic test may therefore be considered quite as reliable as most experimental biologic tests and certainly more trustworthy than ordinary zoopharmacologic methods of assay.

EXAMINATION OF WHOLE BLOOD

I have been employing blood serum generally in testing the toxicity of blood from patients with pemphigus because it is usually impossible to secure a specimen of fluid whole blood for such an examination without the use of a chemical anticoagulant. However, studies can be made with specimens of whole blood from normal and diseased patients in two ways. One method is to draw fresh blood, quickly measure off a definite amount and lake it in plant-physiologic saline solution. Another, more accurate method is to prevent coagulation of blood by the use of highly purified heparin. Serum kept fluid with such ordinary chemicals as citrate, oxalate and the fluorides cannot be used for plant-physiologic experiments. I have found, however, that highly purified heparin (as prepared in the laboratories of Hynson, Westcott & Dunning), even in concentrations greater than that required to keep the blood fluid, has practically no toxicity for Lupinus albus seedlings. Specimens of whole blood drawn from patients and kept fluid with pure heparin yield phytotoxic indexes of from 65 to 70 per cent, i. e., from 5 to 10 points lower than those given by specimens drawn from normal subjects. Fresh whole blood from patients with pemphigus, when examined in the same way, also gives readings from 5 to 10 points lower than those obtained with serum from patients with pemphigus.

EXPERIMENTS WITH DRY BLOOD

I have recently instituted studies of a new character with specimens of dry blood, of which I expect to make considerable future use. The procedure employed is as follows: Fresh blood is drawn from patients and kept fluid with highly purified heparin. Glass microscopic slides are washed and dried, and over each slide is spread 0.25 cc. of fluid

heparinized blood, which is allowed to dry at room temperature. After the films of blood have dried, the slides are put in separate envelops and preserved either at room temperature or in the icebox at 15 C. Phytopharmacologic studies are made with two dry blood films (equivalent to 0.5 cc. of fluid blood) dissolved in 50 cc. of Shive's solution. Such studies of specimens of dry blood from normal subjects and from those suffering from pemphigus or some other disease have been found to yield phytotoxic readings almost identical with those given by the fresh fluid whole blood tested at the time the dry films were prepared. In this way it was found that the dry specimens of blood from patients with pemphigus retained their toxicity for three months, the maximum age of the dry specimens employed up to the time of writing. It will undoubtedly be found that these dry specimens retain their toxicity for much longer periods. This relative stability of films of dry blood

TABLE 2.—*Phytopharmacologic Examination of Dry Blood Films Dissolved and Compared with Fresh Blood*

Phytotoxic Index of Whole Blood from Normal Subjects (Heparinized)		Phytotoxic Index of Whole Blood from Patients with Pemphigus (Heparinized)	
(Fresh blood fluid	65%)	(Fresh blood fluid	56%)
Dry film two days old	65%	Dry film two days old	53%
Dry film four weeks old	67%	Dry film four weeks old	53%
Dry film eight weeks old	60%	Dry film eight weeks old	52%
Dry film ten weeks old	66%	Dry film ten weeks old	58%
Dry film three months old	67%	Dry film three months old	56%
Average of dry films	65%	Average of dry films	55%

contrasts strikingly with the rapid deterioration of specimens of fluid blood obtained from patients with pemphigus. As I have already stated, the latter decompose rapidly on exposure to light and especially to room temperatures. A comparison of films of dry heparinized blood with samples of whole blood, taken from the same subjects, frozen solid and kept in cold storage, revealed that the dry blood retained its toxicity for a much longer period than did the thawed-out specimens. This investigation is still in progress, but the results already obtained indicate that the dry film may be useful in future phytopharmacologic work, and they suggest, moreover, a method which may be advantageously employed in connection with medicolegal problems (table 2).

COMMENT

I have made a résumé of the phytopharmacologic technic employed in studying specimens of blood from normal and diseased subjects, particularly those from patients with pemphigus. It must be emphasized that in order to perform the phytopharmacologic test successfully the investigator should be trained not only in the experimental methods of zoopharmacology but also in those of plant physiology. Details of

technic can be learned only by practice, and, as is the case in all new laboratory procedures, negative results count for little as far as reliability of the test is concerned.

Four salient features should be emphasized in connection with the phytopharmacologic test. First, the germinating medium should be freed from acids and fungi and should contain the optimum amount of moisture for the maximum germination of healthy seedlings. Second, such exactness as is obtained only by practice should mark the measurement of the seedlings employed for the test. In all cases, measurement of the roots at the beginning and at the end of the experiment should be made by the same person. Third, to insure the most reliable results, seedlings with roots measuring from 35 to 50 mm. should be matched as closely as possible in the various rows of tubes in which the solutions to be examined are kept. Fourth, temperature, the most important ecologic factor, should be rigidly standardized and controlled to insure results comparable with those obtained by the original investigators.

In order to prevent hemolysis and rapid decomposition of red blood cells in specimens from patients with pemphigus, the blood serum, which is generally the most convenient fluid for clinical examination, should be separated early from the whole blood. When whole blood is to be studied it should be kept fluid with highly purified heparin, and no other anticoagulant should be added. In a new study on dry heparinized blood I have found that such specimens from patients with pemphigus allowed to dry at 70 F. retain their toxicity much longer than specimens of fluid blood. Studies on dry blood are of interest from a scientific point of view, because they indicate a convenient method of preserving blood without putrefaction, and also from the practical standpoint, because they suggest a new diagnostic procedure in doubtful pathologic and medicolegal cases.

SUMMARY

A detailed description of my method for determining the phytotoxic index of blood from patients with pemphigus is presented.

The principal factors playing rôles in the modification of phytopharmacologic reactions are discussed.

A complete statistical analysis of a major experiment on a large number of seedlings is given as an illustration.

A new method for detecting pemphigus toxin in films of dry blood, which is of both scientific and practical value, is described.

EFFECT OF OILS CONTAINING UNSATURATED FATTY ACIDS ON PATIENTS WITH DERMATITIS

WITH A BRIEF REPORT OF AN EXPERIMENTAL STUDY IN GUINEA-PIGS

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For the past five or six years a number of investigators have been studying the effects of the feeding of oils containing highly unsaturated fatty acids (with a high iodine number) to patients with infantile eczema and chronic dermatitis (atopic eczema, generalized neurodermatitis).

A. E. Hansen,[1] who was originally responsible for the idea of feeding children oils containing unsaturated fatty acids for infantile eczema had his inspiration from the experiments of Burr and Burr,[2] who noted a cutaneous disease in rats having a deficiency in unsaturated fatty acids. Hansen found low iodine numbers for the serums of patients with infantile eczema and noted a rise of these iodine numbers coincident with clinical improvement which followed feeding of corn oil or linseed oil. He also noted that clinical improvement was accompanied or preceded by a return of the iodine number of the fatty acids in the serum from subnormal to normal levels in some infants who received therapy with crude coal tar,[3] and he suggested this change as the possible mechanism of the therapeutic effect of the tar.

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1. Hansen, A. E.: Study of Iodine Number of Serum Fatty Acids in Infantile Eczema, Proc. Soc. Exper. Biol. & Med. **30**:1198, 1933; Serum Lipid Changes and Therapeutic Effects of Various Oils in Infantile Eczema, ibid. **31**:160, 1933.

2. Burr, G. O., and Burr, M. M.: A New Deficiency Disease Produced by the Rigid Exclusion of Fat from the Diet, J. Biol. Chem. **82**:345, 1929; On the Nature and Rôle of the Fatty Acids Essential in Nutrition, ibid. **86**:587, 1930.

3. Hansen, A. E.: Possible Mechanism of Crude Coal Tar Therapy in Infantile Eczema, Proc. Soc. Exper. Biol. & Med. **31**:161, 1933.

Faber and Roberts [4] in their studies of infantile eczema have also reported on the serum lipids with special reference to saturation of the fatty acids. They found in persons with eczema a cholesterol content slightly higher, a total fatty acid and total lipid content considerably higher and an iodine number for the fatty acids moderately lower than those of the average person. They did not find the degree of unsaturation of fatty acids as far from normal as did Hansen, and they expressed the belief that the findings were secondary rather than etiologic. In the Children's Clinic of the Stanford University Medical School no benefit followed the treatment of infantile eczema by feeding corn oil.

Cornbleet [5] in a preliminary report stated that favorable effects from the assimilation of refined maize oil were observed in chronic eczema which had previously resisted treatment. He emphasized the long time required for permanent results to be established, stating that the average time necessary to achieve a clinical cure is from twelve to eighteen months. He expressed the belief that the action of the maize oil in eczema is due to its high content of unsaturated fatty acids.

Taub and Zakon [6] made some purely clinical studies of the use of unsaturated fatty acids in the treatment of eczema (atopic dermatitis, neurodermatitis) and reported that in none of their patients could they see any improvement in the clinical appearance of the eczema which might be attributed to the taking of linseed oil. They expressed the belief that the promiscuous use of linseed oil, as advocated by its distributors, is entirely unjustified. Furthermore, oil therapy is not without danger to a patient who may be hypersensitive to cottonseed or linseed oil.

In our clinical investigations seventeen patients with chronic dermatitis were fed oils containing highly unsaturated fatty acids daily over periods ranging up to one year or more. The adults were fed 2 ounces (60 cc.) daily of raw linseed oil because of its high iodine number (175 to 202). The dose had to be cut down frequently on account of gastro-intestinal upsets but was soon resumed in full. When linseed oil was not tolerated, cod liver oil (iodine number 137 to 166) was substituted. The patients with infantile eczema received either cod liver oil or corn oil (iodine number 111 to 128) daily in divided doses totaling

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4. Faber, Harold K., and Roberts, Dorothy B.: (*a*) Serum Proteins and Lipoids in the Eczema of Infants and Children, J. Pediat. **3**:78, 1933; (*b*) Studies in Infantile Allergic Eczema: Serum Lipids, with Special Reference to Saturation of the Fatty Acids, ibid. **6**:490, 1935.

5. Cornbleet, Theodore: Use of Maize Oil (Unsaturated Fatty Acids) in the Treatment of Eczema, Arch. Dermat. & Syph. **31**:224 (Feb.) 1935.

6. Taub, Samuel J., and Zakon, Samuel J.: The Use of Unsaturated Fatty Acids in the Treatment of Eczema, J. A. M. A. **105**:1675 (Nov. 23) 1935.

from ½ to 1 ounce (15 to 30 cc.). Various types of culinary ingenuity were necessary in order to make the oil either palatable to the patient or tolerable by his gastro-intestinal tract.

Eleven of the adult patients afflicted with chronic dermatitis (generalized neurodermatitis, atopic eczema) were ambulatory and cooperative in taking the oil prescribed. In seven the condition showed no remarkable change while the oil was being administered; in three there was improvement, and in one cure continued as long as the oil was taken, relapse followed when it was not and improvement ensued when it was resumed. Repeated studies of the blood lipids were made at fairly regular intervals on these subjects during their course of treatment with oil. These studies showed no consistent unusual changes and certainly none that could be said to parallel the clinical condition of the patient.

Six of the patients with infantile eczema who were fed oil were hospitalized. Four of them showed improvement when given the oil, while two showed no remarkable change. Two other patients with infantile eczema who did not receive the oil but were otherwise similarly treated also showed improvement.

METHODS

(a) *Determinations of Blood Lipids.*—The alcohol-ether extract was prepared from 3 cc. of serum diluted to a total volume of 50 cc. This extract allowed 15 cc. for the determination of total fatty acids and cholesterol, 20 cc. for the estimation of the iodine number and from 7 to 8 cc. for the determination of phospholipid phosphorus. Whenever possible, duplicate extractions were made.

After saponification of the alcohol-ether extract, the fatty acids were determined by the oxidative procedure of Bloor,[7] cholesterol by Bloor's[8] adaptation of the Liebermann-Burchard reaction to color and the iodine number by Yasuda's[9] modification of Rosenmund and Kuhnhenn's[10] method. Phospholipid phosphorus was determined directly on the alcohol-ether extract according to the method of Man and Peters.[11]

The values obtained by using these methods are comparable with those obtained by the methods of Hansen[1a] and Faber and Roberts.[4b]

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7. Bloor, W. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53, 1928.

8. Bloor, W. R.: The Determination of Cholesterol in Blood, J. Biol. Chem. **29**:437, 1917; footnote 7.

9. Yasuda, M. J.: The Determination of the Iodine Number of Lipids, J. Biol. Chem. **94**:401, 1931.

10. Rosenmund, K. W., and Kuhnhenn, W.: Eine neue Methode zur Jodzahlbestimmung in Fetten und Oelen unter Verwendung von Pyridinsulfatdibromid, Ztschr. f. Untersuch. d. Nahrungs. u. Genussmittel **46**:164, 1923. Page, I. H.: Pasternak, L., and Burt, M. L.: Ueber den Transport von Fetten und Lipoiden durch Blut nach Oleingabe, Biochem. Ztschr. **223**:445, 1930.

11. Man, E. B., and Peters, J. C.: Gravimetric Determination of Serum Cholesterol Adapted to the Man and Gildea Fatty Acid Method, with a Note on the Estimation of Lipoid Phosphorus, J. Biol. Chem. **101**:685, 1933.

(b) *Experimental Observations.*—The entire question of the relation of dermatitis, atopic eczema and neurodermatitis to the allergic state remains unsettled. In the hope of gaining some information on the subject, we studied the effect of the feeding of oils containing highly unsaturated fatty acids to specifically sensitized animals.

Accordingly, guinea-pigs made sensitive to horse serum by three intracutaneous injections of 0.4 cc. each at intervals of five days were fed daily a highly refined corn oil (iodine number 113 to 125). They received from 5 to 10 cc. daily by mouth or by esophageal catheter, in addition to their stock diet of oil and fodder.

Comparative Experimental Studies

Group Studied	Values Observed by Ourselves Average Initial Values: Iodine Number	Total Lipid, Mg. per 100 Cc.	Total Fatty Acids	Cholesterol, Mg. per 100 Cc.	Clinical Effect of Feeding Oil
8 patients with infantile eczema (hospitalized)	114	547	372	175	4 improved 2 showed little change 2 improved (no oil)
8 infants without dermatoses (hospitalized)	115	528	365	163	
18 adults with generalized neurodermatitis (hospitalized)	120	537	351	186	3 improved 1 cured as long as on oil 7 showed little change
4 adults with other extensive dermatoses (2 children with chronic lesions, 2 with acute lesions, ambulatory)	123	630	402	228	
2 adults with xanthoma diabeticorum and definite metabolic disturbance	130	1,353	830	523	
3 healthy adults without dermatoses	116	575	386	189	
Values Observed and Reported by Hansen [1a]					
6 normal infants	111	546	361	185	
7 patients with infantile eczema	84	488	342	147	All improved when put on oil
Values Observed by Faber and Robers [4b]					
16 normal infants and children	117	451	290	161	
15 infants and children with eczema	107	516	351	168	No benefit from corn oil feeding

Note.—Repeated determinations of lipoid phosphorus were made on our subjects along with the studies of other lipids, but they also revealed no characteristic significant alterations.

After seventeen days of feeding they were shocked by intravenous injection of from 0.2 to 0.6 cc. of horse serum, and their reactions were noted. Every reaction was fatal at once, and in no instance could we feel that the allergic response was in any way mitigated.

A second group of twelve guinea-pigs was sensitized to horse serum in the same way and given the routine diet for fifteen days. After this six were fed daily rations of a mixture of oats and raw linseed oil (iodine number 175 to 205), and six, a mixture of oats and cod liver oil (iodine number 167). The mixtures were replenished every other day, and greens were added once a week. The mixtures were readily consumed by the guinea-pigs, and appreciable gains in weight were noted during the course of the experiment.

At the end of six and one-half weeks of feeding oil these animals were shocked with horse serum as the previous group had been. Again fatal anaphylactic shock was noted in every instance. Control animals which had been fed similarly but not treated previously with horse serum did not show anaphylaxis.

COMMENT

It is well known that certain nonspecific agents can influence the allergic state. These substances may be injected intracutaneously, subcutaneously or intravenously and in rare instances may be given by mouth. Longcope noted the variations in reactions in rats fed on protein as compared with those on diets free from protein. Urbach prevented or greatly reduced the anaphylactic response by feeding substances obtained by peptic digestion of the proteins of certain foods of animal or vegetable origin ("propeptans"[12]). If the dermatoses are allergic and if the efficacy of feeding oil in clinical cases is due to an alteration in the reactivity of the allergic state, these brief experiments with guinea-pigs fail to bear it out.

From the table it is apparent that we found no great difference between the values for patients with neurodermatitis or infantile eczema and those for normal subjects or those not having apparent metabolic disease. In this respect our findings differ from those of Hansen,[1] who observed low iodine numbers in patients with infantile eczema.

A number of our patients who received oil showed rapid gain in weight, but this was naturally to be expected from the relatively great increase in caloric intake. Several of the patients noted increased power of endurance, probably associated with their gain in weight, but no change in their dermatitis. In patients to whom cod liver oil was administered the presumably additional nonspecific effects due to an increased supply of vitamins did not appreciably alter the course of the dermatitis. The results of the therapeutic trials which we have made are perhaps somewhat difficult to evaluate finally and definitely and are perhaps complicated by the fact that many of the patients received additional treatment directed toward local improvement or protection of the skin. We believe, however, that the results observed in the patients who received the oil do not vary at all from those found in similar patients who received no such treatment or any other treatment.

SUMMARY AND CONCLUSION

Repeated studies of the blood lipids were made on subjects to determine the effect of ingestion of oils containing unsaturated fatty acids

12. Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association, 1933, p. 144.

in patients with chronic dermatitis. Our observations give us no reason to believe that there was any characteristic abnormality of the blood lipids in the patients whom we treated or that any specific benefit arises from feeding such patients oils containing highly unsaturated fatty acids.

Prolonged administration of unsaturated oils to guinea-pigs which had been sensitized to horse serum did not prevent anaphylaxis following injection of horse serum.

Dr. S. William Becker assisted us with suggestions. Dr. W. W. Swanson helped in gathering clinical material for the pediatric studies.

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KLINE EXCLUSION TEST IN PREVENTION OF TRANSFUSION SYPHILIS

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The proper selection of a blood donor necessitates not only tests for compatibility of blood and physical examinations but also, immediately before the transfusion, a very sensitive blood test for syphilis to prevent the transmission of this disease. The Kline exclusion slide test is an excellent method for this purpose, even in emergency cases, because of the rapidity, simplicity and ease of its performance and its high degree of sensitivity.

Fifty-nine cases [1] in which syphilis has been transmitted by donors are already recorded in medical literature! The actual number is probably much greater. In most of the cases reported serologic and physical examinations of the donors either were not made at all or else were not made within from three to twelve weeks prior to the transfusion. Professional donors, especially those used in cases of emergency, usually fall in the latter category, while voluntary donors, especially friends and relatives, owing to a feeling of delicacy, usually fall into the former.

From the Department of Laboratories of the Mount Sinai Hospital.

1. (*a*) Jones, H. W.; Rathmell, T. K., and Wagner, C.: The Transmission of Syphilis by Blood Transfusion, Am. J. Syph. & Neurol. **19**:30-38 (Jan.) 1935. (*b*) Brem, W. V., in discussion on Griffin, H. Z., and Haines, S. F.: A Review of a Group of Professional Donors, J. A. M. A. **81**:532 (Aug. 18) 1923. (*c*) Périn, L., and Lefèvre, M.: Transmission de la syphilis par voie sanguine, Nourrisson **23**:371-374 (Nov.) 1935. (*d*) Mandelbaum, H., and Saperstein, A. N.: Transmission of Syphilis by Blood Transfusion: Case of Acute Gummatous Osteomyelitis, J. A. M. A. **106**:1061-1063 (March 28) 1936. (*e*) Polayes, S. H., and Lederer, M.: The Transmission of Syphilis by Blood Transfusion, Am. J. Syph. **15**:72-80 (Jan.) 1931. (*f*) Post, C. D., and Cooney, G. C.: Accidental Transmission of Syphilis by Blood Transfusion, J. A. M. A. **100**:258-259 (Jan. 28) 1933. (*g*) Feldman, V. J.: Syphilis D'Emblée, Arch. Dermat. & Syph. **18**:380-382 (Sept.) 1928. (*h*) Cummer, C. L.: Transfusion Syphilis, Am. J. M. Sc. **185**:787-789 (June) 1933. (*i*) Morgan, H. J.: Factors Conditioning the Transmission of Syphilis by Blood Transfusion, ibid. **189**:808-813 (June) 1935. (*j*) Williamson, G. R., and Strong, R. A.: Congenital Syphilis from Blood Transfusion to the Mother During Pregnancy, Am. J. Syph. **17**:484-491 (Oct.) 1933. (*k*) Hendrick, H.: Diseases Transmitted in Blood Transfusion, Proc. Inst. Med. Chicago **10**:185-195 (Jan. 15) 1935. (*l*) Aubertin, C., and Fleury, J.: Syphilis après transfusion sanguine, Bull. et mém. Soc. méd. d. hôp. de Paris **54**:69-75 (Jan. 27) 1930.

This laxity in the examination of donors is well exemplified by the following excerpt from the report of one of the large hospitals in the east: [2]

> Each time a donor reports for a transfusion, a hemoglobin determination is made, and some of his serum is saved for a Wassermann. A Wassermann test cannot be done immediately preceding each transfusion, and even if it could be done, it is still theoretically possible to transmit the infection.

In some cities in the United States organizations for the control of professional donors have sprung up. A representative one in New York [3] furnishes "properly certified" donors for patients in need of transfusions at a nominal cost, taking the responsibility for a service which formerly had been under the control of commercial agencies. The donors are examined by physicians of this organization for physical fitness, accessibility of veins, type of blood, and serologic freedom from syphilis. All these facts are recorded in a pass-book, which the donor carries and presents when called to give a transfusion. The Wassermann reaction is determined once every six months, and the Kahn precipitation test is done at like intervals, the two being alternated so that the blood of donors is examined every three months. Such serologic control is obviously unsatisfactory, since the greatest danger is from donors in the primary and secondary stages of syphilis in this very three month period.

Reports not only in the United States but in foreign countries, such as France, [1c] Great Britain,[4] Germany,[5] Republic of Panama [6] and the Union of Soviet Socialist Republics,[1g] indicate the same inadequacy in the serologic control of donors. The following quotation concerning the present naïvely conducted "organization of blood donors in Germany" likewise indicates the unsatisfactory control of donors in that country:

> Only donors of pure Aryan ancestry are accepted—as a rule only students or members of the National Socialist Party. Donors are reexamined every three months in Leipzig and Frankfort-on-the-Main, and every two months in Berlin and Vienna. When reexamined the donor must state in writing, on his word of honor, that in the meantime neither he nor any member of his family has been infected with syphilis or any other infectious disease. No examination is made prior to the transfusion.[5]

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2. Martin, H. E., and Whyte, R.: Organization of Transfusion Service and Blood Donors Bureau for Average Hospital, Am. J. Surg. **32**:439-444 (June) 1936.

3. Corwin, E. H. L.: Community Control of Professional Blood Donors, New York State J. Med. **35**:317-320 (April 1) 1935.

4. Keynes, G.: The Technique of Blood Transfusion and the Organization of a Public Transfusion Service, J. State Med. **41**:685-707 (Dec.) 1933.

5. Organization of Blood Donors in Germany, Foreign Letters, J. A. M. A. **105**:610-611 (Aug. 24) 1935.

6. McNamara, W. L.: The Noninfectivity of the Blood in Tertiary Syphilis, Am. J. Syph. **9**:470-478 (July) 1925.

Several recent reports [7] call attention to the need for more rigid serologic control and for examination of the donor shortly before transfusion. The question resolves itself into one of the proper time for the examination to take place and of the serologic test to be used. Feldman [1g] suggested the performance of a serologic test every month and again before the transfusion. Jones and his associates [1a] suggested the use of the Kahn test, which requires "only two hours for its performance," on the day of the transfusion. Cummer [1h] suggested the use of the Kline microscopic precipitation test on blood from the finger immediately before the transfusion, referring to the experience of Eller and Rein [8] with this particular test.

The diagnosis of syphilis serologically is difficult in two stages: (1) in very early primary syphilis, as in the cases reported by Brem [1b] and Post and Cooney,[1f] and (2) in insufficiently treated or old tertiary syphilis. McNamara [6] successfully transfused blood from persons with old tertiary syphilis into a number of patients without transmitting the disease, and he concluded that it is safe to use such donors. On the other hand, the experience of Mandelbaum and Saperstein [1d] and others indicates that the disease may be and has been transmitted by such donors. With the less sensitive complement fixation and precipitation tests especially, cases of early primary, old tertiary and insufficiently treated syphilis have been overlooked.

As shown in the recent evaluation of blood tests for syphilis in the United States by the American Society of Clinical Pathologists and the United States Public Health Service,[9] the Kline exclusion slide test (performed by Rein) gave results of maximum sensitivity in the group of tests, with less than 1 per cent of false positive reactions. In its conclusions the committee suggested the routine use of a properly performed, highly sensitive flocculation test to exclude the presence of syphilis. Because of its maximum sensitivity, its satisfactory specificity and the rapidity, simplicity and ease of its performance, the Kline microscopic precipitation test is most satisfactory and especially applicable for the purpose of excluding donors with syphilis immediately before the transfusion.

In the laboratories of the Mount Sinai Hospital of Cleveland, a large list of professional donors is always maintained, and from this donors are supplied not only for that hospital but also for several of the smaller

7. Jones.[1a] Feldman.[1g] Cummer.[1h] Hendrick.[1k]

8. Eller, J. J., and Rein, C. R.: Kline Finger Blood Precipitation Test for Syphilis, Arch. Dermat. & Syph. **25**:238-244 (Feb.) 1932.

9. Cumming, H. S.; Hazen, H. H.; Sanford, A. H.; Senear, F. E. M.; Simpson, W. M., and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States, Ven. Dis. Inform. **16**:189-201 (June) 1935; supp. 1, June 1935, pp. 1-49.

hospitals in the city. Professional and voluntary donors are treated alike. Their blood is typed, a Tallqvist determination of the hemoglobin is done, diagnostic and exclusion slide tests are performed and an adequate physical examination is made. In the past six years, in over 1,500 blood transfusions, not one case of syphilis has been transmitted at this hospital.

Ordinarily both the diagnostic and the exclusion Kline test [10] with heated serum are done. A test tube containing clotted blood is brought to the laboratory at the same time as the saline suspension of cells for typing and direct matching. The blood is centrifugated while the materials for the typing are secured and set up. The clear supernatant serum is then placed in a hot water bath, at 56 C., for thirty minutes. During this interval the typings and direct matchings are done. If the donor has the proper type of blood and if his cells do not agglutinate on direct matching, the slide tests are then performed. These require only an additional five minutes: one-half minute to measure out the 0.05 cc. of serum into each of the paraffin-ringed slides and to add the diagnostic and exclusion emulsions (these are satisfactory for use for forty-eight hours and are always on hand rather than prepared just before use), then four minutes to rotate and one-half minute to read the results. This procedure does not materially delay the most urgent transfusion and is easily done at any time of the day or night.

The advisability of testing the blood of donors immediately before use is obvious. For example, there have been numerous cases in which a prospective donor was excluded on the basis of a strongly or a weakly positive serologic reaction. In the laboratory of the Mount Sinai Hospital any person who shows a reaction even slightly positive in the exclusion test is declared unsatisfactory as a donor.

A certified professional donor from New York presented his pass-book at the laboratory and declared himself ready to go to work. Despite his credentials, he was treated like all other prospective donors, and his serologic reaction was found to be strongly positive. This incident occurred within that three month period between serologic examinations of professional donors as established in New York and elsewhere and is proof that the system is decidedly inadequate.

D. C., a white man aged 21, came to us on June 13, 1933, and offered to be a professional donor. He was physically fit and had readily accessible veins. His blood was type IV (Moss classification). He came quickly when called for emergencies. For these reasons he was well liked, and we used him frequently during the following year and a half. On Dec. 26, 1934, he was called late at night. When he arrived it was

10. Kline, B. S.: Microscopic Slide Precipitation Tests for the Diagnosis and Exclusion of Syphilis, Baltimore, Williams & Wilkins Company, 1932.

noticed that the cervical lymph nodes were enlarged. On inquiry he said he did not have a sore throat and protested that he was well enough to give blood for the transfusion. His serologic reaction, however, was 4 plus in both diagnostic and exclusion tests. Further examination showed a lesion on the lip, and in a smear from this lesion numerous typical spirochetes (Spirochaeta pallida) were detected. Such a person, known as a reliable professional donor and used only a few weeks previously, might well have given syphilis to the recipient of the transfusion had he not been excluded by careful serologic control.

Rein, who has been actively supporting a similar procedure in New York, reported in a recent article,[11] that a number of the large hospitals and a large agency[12] for professional donors there are rechecking donors serologically by means of the Kline exclusion slide test immediately before transfusions. The result of this action can only be beneficial, and similar control should be established universally.

CONCLUSION

The proper selection of a donor necessitates not only tests for compatibility of blood and physical examinations but also, immediately before the transfusion, a very sensitive blood test for syphilis, to prevent the transmission of the disease. The Kline exclusion slide test is an excellent method for this purpose, even in emergency cases, because of the rapidity, simplicity and ease of its performance and its high degree of sensitivity.

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11. Rein, C. R.: The Value of the Kline Exclusion Test in the Serodiagnosis of Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **20**:515-522 (Sept.) 1936.

12. Rein, C. R.: Personal communication to the author on the certification of blood donors in Jamaica, N. Y.

KERATOSIS BLENNORRHAGICA WITH CORNEAL LESIONS

FURTHER OBSERVATIONS ON THE THERAPEUTIC EFFECT OF HYPERPYREXIA

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The previously reported successful therapy of keratosis blennorrhagica by one of us (E. E.[1]) has prompted this further study of the effect of artificial hyperpyrexia in the treatment of this disease. The technic was fully described in the previous communication and need not be reviewed. It suffices to state that it is a minor variation of the blanket method employed by Norman Epstein and Maurice Cohen [2] in the treatment of syphilis. The rarity of gonorrheal keratoses renders the presentation of small series of value in the establishment of this therapeutic agent. The cases reported are also noteworthy because of the association of corneal lesions with the keratosis.

REPORT OF CASES

CASE 1.—G. F. M., a man aged 22, in 1929 had polyarthritis which followed a purulent discharge from the left ear. Although there was no history of syphilitic lesions, a diagnosis of syphilis was made. Treatment consisted of weekly injections in the arm and in the hip. After the patient had received approximately thirty of each, he was pronounced well. A urethral discharge was not noted.

In May 1935 urethritis and conjunctivitis developed. According to the patient, no attempt was made to establish the etiology of this condition. In October his left knee and ankle became acutely swollen, tender and painful. He entered an osteopathic hospital where futile attempts were made to demonstrate gonococci in smears of material from the urethra and conjunctiva as well as in the pus aspirated from the knee. Kolmer, Kahn and Kline tests of the blood were all reported to show 4 plus reactions. The sedimentation rate of the erythrocytes was rapid, twenty-three minutes being required for the line of demarcation to reach the 18 mm. mark. A routine urinalysis gave negative results, and except

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1. Epstein, E.: Hyperpyrexia in the Treatment of Keratoderma Blennorrhagicum, Am. J. Syph., Gonor. & Ven. Dis. **21**:148 (March) 1937.

2. Epstein, N. N., and Cohen, M.: The Effects of Hyperpyrexia Produced by Radiant Heat in Early Syphilis, J. A. M. A. **104**:883 (March 16) 1935.

for a leukocyte count of 14,100 per cubic millimeter with 72 per cent polymorphonuclears, the blood count was normal.

During the two and one-half months the patient spent in the hospital he had a remittent elevation of temperature that attained a daily maximum of between 100 and 102 F. At this time, pains developed in both shoulders and hips. Thick crusts appeared on the soles of both feet. These were so dense that he was unable to remove them. An osteopathic "dermatologist" was consulted, and he offered a diagnosis of "epidermatophytosis" without performing a microscopic examination of the crusts after immersion in potassium hydroxide. Neither biopsies nor cultures were made.

The patient received weekly injections of neoarsphenamine and of bismo-cymol, and his symptoms gradually subsided. Except for intermittent pain in the left ankle, he offered no complaints until May 20, 1936. At that time he again suffered from conjunctivitis and urethral discharge. Five days later he noticed slight swelling accompanied by severe pain and tenderness in the regions of the left knee and of both ankles. Simultaneously, a few pustules appeared on both feet, and four days later the patient entered the Los Angeles County Hospital.

At the time of his entry his temperature was 100.6 F. The conjunctivae were markedly injected, and a mucopurulent discharge was present. Both corneas were normal. The lids were swollen and reddened. The teeth were in poor condition. Several concentric white papules were seen on the roof of the mouth. A number of hyperkeratotic pustules, some coalescing and some discrete, were present on the penis. A purulent urethral discharge was noted. Both ankles and the left knee were tender but not particularly swollen. Pain limited the motion of the affected joints. On both dorsa and the soles of the feet were a number of discrete pustules, each having an intensely hyperemic areola (fig. 1). Some of the lesions were commencing to dry and displayed a brownish center. Several subungual pustules were also present. Several pustules had coalesced to involve the major portion of the left big toe and of the adjacent interdigital space. The hands were not affected.

Smears of purulent material obtained from the eye, from the urethra and from lesions on the feet failed to reveal gonococci. A microscopic section of an early pustule stained by the method of Krajian [3] showed no organisms. The Kolmer reaction of the blood was 4 plus, while the Kahn reaction was only 1 plus. Three blood cultures failed to demonstrate a bacteremia. The nonprotein content of the blood was 50 mg. per hundred cubic centimeters, while the apparent creatinine was 1.9 per cent by volume. The icterus index was 9, and both the direct and the indirect van den Bergh reaction were negative. A urinalysis gave negative results. A lumbar puncture was performed, but examination of the cerebrospinal fluid revealed no abnormalities.

During the two weeks the patient was under observation, he received only acetylsalicylic acid, cod liver oil and malt and two injections of 0.13 Gm. of bismuth subsalicylate. He had a remittent rise of temperature, with daily peaks of from 100 to 101 F.

Histopathologic Examinations.—A number of biopsies were performed, and the tissues were fixed in diluted solutions of formaldehyde U.S.P. (1:10) and stained with hematoxylin and eosin. The observations were consistent with the diagnosis of keratosis blennorrhagica. The majority of the histopathologic studies

3. Krajian, A. A.: A Rapid Method of Staining Spirochaeta Pallida in Single Sections of Tissue, Arch. Dermat. & Syph. **32**:764 (Nov.) 1935.

were performed on early lesions in a futile attempt to demonstrate vesiculation, said to be the primary lesion in this process.[4]

The corneum showed only hyperkeratosis. In one section the stratum lucidum and the stratum granulosum were slightly thickened, but in the remainder these layers were not prominent. A section from an acute abscess is shown in figure 2. Here the corneum forms the roof while the invaginated, thinned prickle cell layer forms the sides and floor. The contained cells are predominantly polymorphonuclear leukocytes, although an occasional lymphocyte may be noted. Besides the aforementioned changes, two further changes were seen in the prickle cell

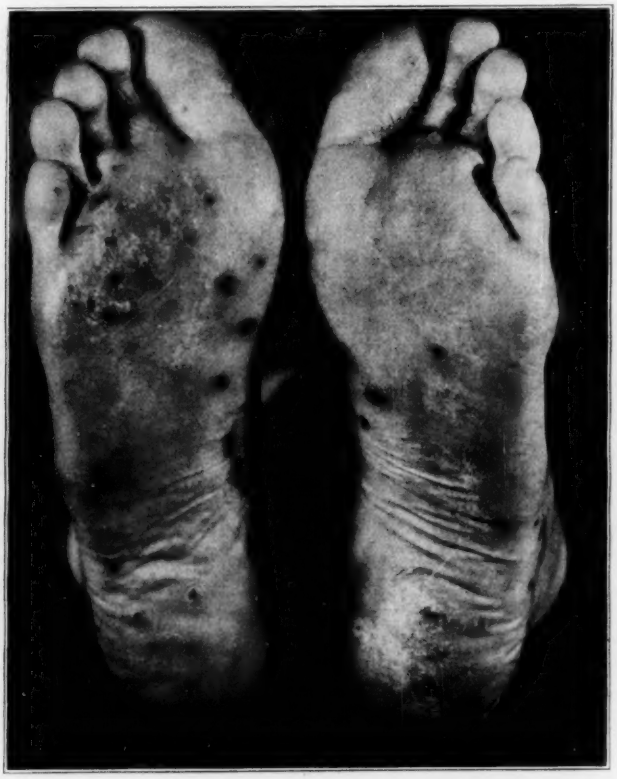

Fig. 1 (case 1).—Early lesions on the soles.

layer. Acanthosis was marked adjacent to the abscess, while in later lesions a moderate, fairly regular elongation of the rete pegs was present. In some sections, inflammatory cells could be seen in the rete. These appeared to be migrating from the corneum to the subcorneal region. The infiltration consisted mainly of mononuclear cells, polymorphonuclear leukocytes being in the minority.

The extent of the edema of the corium varied with the stage of the lesion. The vessels were dilated. A cellular infiltrate was present in all stages and was

4. Keim, H. L.: The Histogenesis of Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.

most marked in the pars papillaris. It consisted predominantly of mononuclear cells and tended to be perivascular. In acute lesions the infiltration was marked, while in later stages it was of minor importance.

Treatment and Course.—Besides the aforementioned measures artificial hyperpyrexia was the only treatment administered. This was instituted on June 10. On this date the temperature was artificially elevated until the oral reading was 106.6 F. and was maintained above 104 F. for four and one-quarter hours. The following day the involved joints were markedly improved, and the lesions on the penis and those in the mouth were definitely regressing. However, those on the feet were slightly accentuated.

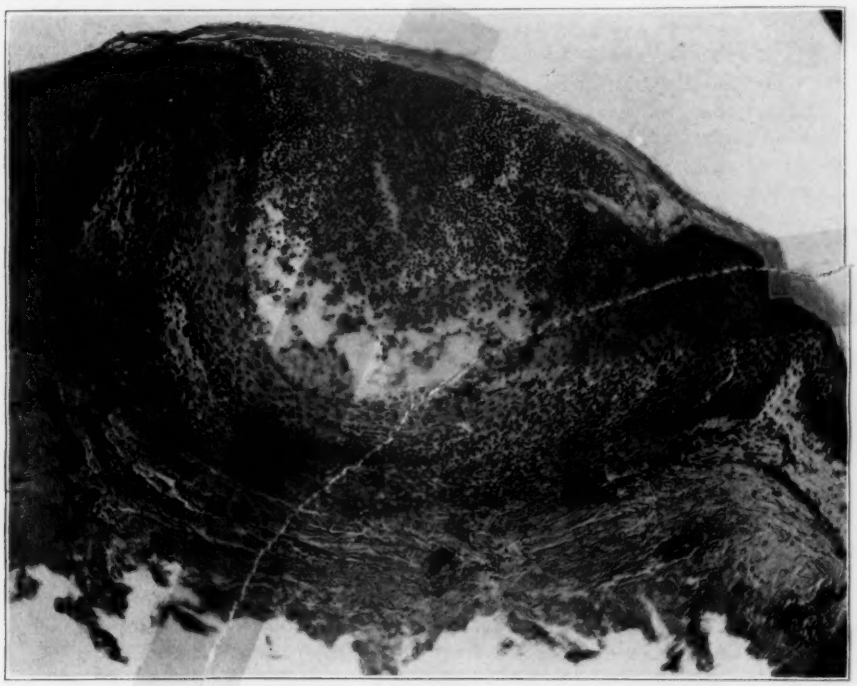

Fig. 2 (case 2).—Section from acute pustule; × 70.

Two days later the temperature was again raised to 106.6 F., but this time the febrile reaction was sustained above 104 F. for five hours. After this treatment all the lesions improved, and those in the mouth completely disappeared, leaving no sequelae. The improvement continued as further treatments were given on June 14 and 16. The first of these was characterized by an acme of 105.6 F., with the temperature remaining above 104 F. for four and one-half hours. In the second the temperature reached 106 F. and remained above 104 F. for four and three-quarter hours. During the fifth treatment, which was given on June 19, the patient became markedly delirious when the temperature had risen to 104.4 F., and this necessitated the termination of the treatment.

Five days later the patient complained of pain in the right eye, and examination revealed a shallow corneal ulcer. He thought the fever treatments were respon-

sible for this and refused further therapy. Simultaneously, a marked recurrence appeared on the skin. The dorsum of both feet and the lower halves of the legs were literally sprinkled with pinpoint pustules with intense areolae. A few lesions also developed on the hands, the majority being located on the dorsal surface. Hyperkeratotic crusts soon formed. The left elbow coincidentally became swollen, tender and painful. This exacerbation was not accompanied by a spontaneous febrile reaction or by the appearance of new papules in the mouth.

By July 13, the patient was comfortable enough to submit to further hyperpyrexia. On this date his temperature was elevated to 105.8 F. and was maintained at a level in excess of 104 F. for four hours. Immediately the lesions started to regress, and the acute arthritic symptoms were relieved. The eyes returned to normal within forty-eight hours. The urethritis had given him no further trouble since the second fever treatment. He was able to leave the hospital on July 18, being well on his way to recovery.

CASE 2.—A. J. Z., a man aged 31, contracted an acute urethritis in 1926. This responded to conservative therapy. There was no recurrence until Sept. 22, 1936, when a urethral discharge developed after he indulged in an alcoholic debauch. This was accompanied by swelling of the penis, conjunctival injection and severe pain and tenderness in the left wrist, in the right knee and in both ankles. The patient applied a liniment and a hot bake to the right knee. A second degree burn with edema, erythema and the formation of flaccid bullae resulted. Having lost faith in his home remedies, he entered the Los Angeles County Hospital on September 26.

The aforementioned joints were tender, warm and slightly swollen. Motion was limited by the acute pain. The eyes showed moderate swelling of the lids, moderate chemosis and injection of the conjunctivae. There were no corneal lesions at this time. The mucous membranes of the mouth were not involved. The skin over the right knee was erythematous and warm to the touch. There were a few superficial ulcerations and several small pustules in this area. A mild areola surrounded each pustule. Each of the lesions exhibited a brown spot on its summit. The penis was diffusely swollen and reddened. A creamy discharge was easily expressed from the urethra. The right epididymis was swollen, tender and smooth. Physical examination disclosed no other abnormalities.

Examination of the urethral discharge revealed numerous gram-negative intracellular and extracellular diplococci. No organisms were observed in smears of material taken from the eye and from the lesions on the knee. Cultures and serologic examination of the blood for evidence of syphilis gave negative results. The results of routine blood counts and urinalyses were not remarkable.

While he was in the hospital, the patient had a remittent febrile reaction that ascended to from 102 to 103 F. During this time there developed deep lesions at about 6 o'clock on each cornea. These soon reached the surface, and the tops sloughed off, leaving corneal abrasions. These were accompanied by marked ciliary injection. Consulting ophthalmologists considered this process to be identical with that causing the ulcer of the cornea in the first patient. Anterior synechiae formed as a result of bilateral iridocyclitis. An early decubitus ulcer was noticed over the sacrum.

Histopathologic Examination.—Several biopsies were performed. The tissue was fixed in diluted solution of formaldehyde U.S.P. (1:10) and stained with hematoxylin and eosin. The essential pathologic changes were as in case 1. The hyperkeratosis, acanthosis, edema and cellular infiltration were marked. A greater amount of parakeratosis was present than was seen in sections examined in case 1.

Treatment and Course.—Before the patient was seen in consultation by us, he had received two intravenous injections of typhoid-paratyphoid A and B vaccine. The initial dose was 35,000,000 organisms and caused a moderate elevation of temperance. A second dose, of 50,000,000, given three days later, raised his temperature to 103.2 F. After this his joints were slightly improved, and the daily spontaneous febrile reactions became less marked. No further attempt was made to elevate his temperature until two weeks later. On Oct. 19 he was given 75,000,000 organisms intravenously, and when his temperature reached 100.6 F. and showed signs of decreasing, a second dose, of the same size, was administered. By this means, his oral temperature was raised to 105 F. After this, the joints felt somewhat better, and the cutaneous lesions assumed more of a hyperkeratotic aspect, losing much of the acute pustular element that had previously characterized them.

Blanket therapy was started on October 23, and the patient's oral temperature was elevated to 106.8 F. by this method. It was maintained above 104 F. for six consecutive hours. Three days later it was raised to 107 F. and kept above 104 F. for six and one-half hours. At the conclusion of this treatment there developed circulatory collapse which was successfully combated by intravenous injections of a cardiac stimulant (a 25 per cent solution of pyridine betacarbonic acid diethylamine), epinephrine hydrochloride, dextrose and physiologic solution of sodium chloride in conjunction with the use of an oxygen tent. These two paroxysms were sufficient to rid the patient completely of the visible manifestations in the eyes, on the skin and in the genito-urinary tract. The arthritis was greatly improved. Seven further treatments were given by the use of divided doses of typhoid-paratyphoid vaccine. Temperatures ranging up to 105 F. were attained, but it was not possible to maintain a level in excess of 104 F. for longer than forty-five minutes by this method. On December 15 the urethritis recurred and the arthritis became more marked. For the first time, the right shoulder was involved. At the same time, a number of hyperkeratotic pustules appeared on the penis. Histologically, these were consistent with a diagnosis of keratosis blennorrhagica. The penis was also markedly edematous. Between Dec. 28, 1936, and Jan. 6, 1937, four additional blanket treatments were given. During these treatments the temperature was not allowed to exceed 106 F. and on the average was maintained above 104 F. for four and one-half hours. This was sufficient to overcome all clinical signs and symptoms presented by this patient. He was discharged, apparently well, on January 21.

COMMENT

These cases are of interest from the clinical and from the therapeutic standpoint. The development of corneal lesions that were suggestive of those seen on the skin points to a relationship between the two. The lesions in the eye began as deep papules or vesicles which reached the surface of the cornea and became eroded in from twenty-four to forty-eight hours. Pain and photophobia accompanied the process. Both of us have reported the occurrence of papules in the mouth accompanying acute exacerbations of the keratosis.[5] The appearance of

5. Chambers, S. O., and Koetter, G. F.: Keratosis Blennorrhagica, Arch. Dermat. & Syph. **27**:411 (March) 1933. Epstein.[1]

the corneal lesions coincidentally with a recurrence of the cutaneous lesions suggests a phenomenon similar to that producing the lesions in the mouth. In neither of these cases, nor in the first one reported in this series,[1] could gonococci be demonstrated in the cutaneous or ocular lesions by cultures, smears or histologic examinations. According to Barrett [6] gonococci have been observed in four reported cases. Despite this, our experience leads us to the belief that keratosis blennorrhagica is a toxic manifestation of a gonorrheal infection because of the coincidental development of multiple lesions on the skin as well as on the mucous membranes of the mouth and on the eye. Our inability to observe organisms in the hyperkeratotic papules and the association with acute urethritis and arthritis further strengthen this impression.

The localization of the process to a traumatized area in case 2 is unusual. Though the presence of a gonococcic infection was definitely established, the cutaneous lesions were admittedly atypical. This was possibly due to the changes produced by the preceding burn. Both the clinical and the histologic picture could best be described as being consistent with, but not typical of, keratosis blennorrhagica. The penile lesions during the recurrence were, however, typical hyperkeratotic pustules. The disease was seen in all its characteristic manifestations in case 1.

The therapeutic results obtained by hyperpyrexia in these cases were gratifying. As was expected, divided doses of typhoidparatyphoid vaccine administered intravenously did not yield as satisfactory a result as the blanket method. This is probably due to the difference in the height of the temperature attained and in the time it is maintained by these methods. The improvement in these two cases was not as sensataional as that in the first reported case [1] but was satisfactory. When one considers the results of therapeutic fever in other manifestations of gonococcic infection, a rationale for its use in keratosis blennorrhagica is apparent. The experience in case 2 warns that fever therapy is not without danger and should be employed only in hospitals, under strict supervision.

The prompt response in both cases argues that the results obtained were due to the treatment. The keratosis may recur if the blennorrhagic infection is not completely eradicated. For this reason, it is essential that patients with this condition be observed for years. While it is impossible to guarantee the permanence of our results, we have noted immediate relief of the associated arthritis, urethritis and ocular lesions as well as the disappearance of the dermatologic manifestations of the disease. This, in itself, is of undoubted value.

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6. Barrett, C. C.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **22**:627 (Oct.) 1930.

Obviously, three cases are not sufficient to establish the value of a therapeutic agent. However, this second report is offered with the hope that it will serve as an added impetus to others to study the effect of artificial hyperpyrexia in this rare disease. Only in this way can enough cases be collected to establish the degree of efficiency of this treatment.

SUMMARY

Two cases of keratosis blennorrhagica with associated corneal lesions are reported.

The successful results of artificial hyperpyrexia therapy are also described.

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SCLEREDEMA ADULTORUM (BUSCHKE)

REPORT OF CASE INVOLVING THE TONGUE

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Epstein's [1] report of two cases of scleredema adultorum has been the only such article on this disease to appear in the American periodical literature. Since this report, the latest editions of American textbooks [2] have included descriptions of it. Cases have been reported in the transactions of societies by Guy and Amschel [3] and Pillsbury.[4] None of these American sources has mentioned involvement of the oral mucous membranes in the clinical picture. Epstein's [1] summary of the forty-one cases reported in the German and French literature lists four in which the tongue was involved. The following case of classic scleredema adultorum is of interest because involvement of the tongue was an outstanding complaint of the patient.

REPORT OF CASE

J. P., a white man aged 22, consulted me on April 7, 1936, giving the following history: In January 1936, he had a severe attack of tonsillitis, with a temperature of 102 F., and was confined to bed for six days, duing which time the fever and sore throat subsided. The following week there were transitory shooting pains in the back of the neck. These disappeared, and he noticed then, for the first time, that the skin of the neck beneath the jaw was becoming hard. This induration extended rapidly in both directions around to the nape of the neck and then slowly spread over the face, down over the chest and, more recently, to the back. There were no subjective sensations other than the limitation of motion. Movement of the head became restricted first and then opening of the mouth. After this the tongue became involved gradually. It felt stiff and was moved about the mouth with difficulty. The most annoying feature came while eating. Food would lodge on the roof of the mouth, and the patient would be forced to use his finger to push it back so that it could be swallowed. There was no difficulty in the act of swallowing after food reached the posterior part of the pharynx. Recently he had noted difficulty in taking a deep breath (costal breathing).

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1. Epstein, N. N.: Scleredema Adultorum (Buschke), J. A. M. A. **99**:820 (Sept. 3) 1932.

2. Ormsby, O. S.: Diseases of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1934. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935.

3. Guy, W. H., and Amschel, F.: Scleredema, Arch. Dermat. & Syph. **29**: 777 (May) 1934.

4. Pillsbury, D.: Sclerema Adultorum (Buschke), Arch. Dermat. & Syph. **32**:691 (Oct.) 1935.

The general physical examination revealed no abnormality other than large, red, cryptic tonsils, which were seen with difficulty through the partially opened mouth. The skin over the face and neck, the upper parts of the arms, the chest and the back down to the waist was boardlike and hard and could not be picked up between the fingers. It did not pit on firm pressure. There was a slight erythematous flush over the cheeks, neck and shoulders, but no other surface changes. The face had a masklike expression, from obliteration of normal markings and immobility, which involved the eyelids as well as the mouth. The tongue could not be extended beyond the teeth. It felt firmer than normal at the tip and was progressively more involved toward the posterior portion. Nothing definite was felt in the soft palate or uvula. The scalp was firm and immobile. There was no loss of hair.

The temperature and the results of blood counts and of examinations of the urine were not remarkable.

Histologic examination of skin removed from the side of the neck showed the following picture: The epidermis was normal. The upper portion of the corium showed a fine connective tissue, normal in appearance. There was a sparse perivascular round cell infiltration, but there were no changes in the blood vessels themselves. The deep portion of the corium showed swollen, hypertrophied collagen fibers, homogeneous in appearance, and the bundles were separated rather widely by clear spaces.

The patient was observed from time to time. The induration continued to extend for about six weeks, ultimately reaching down the forearms to the wrists, over the abdomen and down the thighs to the knees. The penis and scrotum were not involved. The induration then began to recede slowly, the skin becoming more pliable and movement less restricted, starting at the periphery. The first involved areas were the last to resolve. Examination on Jan. 15, 1937, approximately one year after the onset, showed definite induration remaining about the face and neck. The tongue still could not be extended beyond the teeth, but during the past month it had become more freely movable in the mouth.

Treatment consisted of contrast baths, massage with 3 per cent salicylic acid ointment and application of galvanic current to the neck. The patient said that all these measures, especially the use of the galvanic current, made him feel better. Two roentgen ray treatments of 150 roentgens each through 2 mm. of aluminum were given over the left deltoid region. There was no noticeable effect. The tonsils were removed after the process had subsided to a degree sufficient to allow opening the mouth.

SCLERODERMA AND SCLERODACTYLIA ASSOCIATED WITH INTERMITTENT CLAUDICATION

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During the past few years the etiology of scleroderma has received considerable attention from European and American investigators. Among many of the possible causes, the glands of internal secretion [1] and the sympathetic nervous system [2] have been considered both separately and together as playing important rôles in the production of the pathologic changes noted in this disease. Osler [1i] and Oliver,[3] however, have summed up the actual knowledge as to the source of scleroderma in the statement that little progress has been made in determining its exact cause. Sclerodactylia has been classified as an angiotrophoneurosis related to endocrine disturbance and to dysfunction of the sympathetic nervous system.[4] Sellei [5] has recently suggested dysfunctions of

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1. (*a*) Strunz, F.: Ein Fall von Progeria, beginnend mit ausgedehnter Sklerodermie, Ztschr. f. Kinderh. **47**:401, 1929. (*b*) Strümpell, A.: Ein Beitrag zur Pathologie und pathologischen Anatomie der Acromegalie, Deutsche Ztschr. f. Nervenh. **11**:51, 1897. (*c*) Sequeira, J. H.: Four Cases of Scleroderma Associated with Disease of the Thyroid Gland, Brit. J. Dermat. **28**:31, 1916. (*d*) Longcope, W. T.: Hypoglycemia in Scleroderma: Metabolism in Eight Cases with Reference to Function of Glands of Internal Secretion, J. A. M. A. **90**:1 (Jan. 7) 1928. (*e*) O'Leary, P. A., and Nomland, R.: A Clinical Study of One Hundred and Three Cases of Scleroderma, Am. J. M. Sc. **180**:95, 1930. (*f*) Castle, W. F.: The Endocrine Causation of Scleroderma, Brit. J. Dermat. **35**:255 and 303, 1923. (*g*) Hoffmann, H.: Untersuchungen über endokrine Störungen bei Hautkrankheiten, insbesondere Sklerodermie und Acrodermatitis atrophicans, Acta dermat.-venereol. **6**:423, 1925. (*h*) Foerster, O. H.: Relation of Internal Secretions to Cutaneous Disease, J. Cutan. Dis. **34**:1, 1916. (*i*) Osler, W.: On Diffuse Scleroderma with Special Reference to Diagnosis and to the Use of Thyroid Gland Extract, ibid. **16**:49, 1898.

2. (*a*) Adson, A. W., and Brown, G. E.: Thoracic and Lumbar Sympathetic Ganglionectomy in Peripheral Vascular Diseases: Therapeutic Value, J. A. M. A. **94**:250 (Jan. 25) 1930. (*b*) Baissaud, E.: Pathogénie du processus sclérodermique, Presse méd. **51**:285, 1897. (*c*) Hoffmann.[1g]

3. Oliver, E. L.: Generalized Scleroderma in Children, Arch. Dermat. & Syph. **25**:72 (Jan.) 1932.

4. Hoffmann.[1g] Adson and Brown.[2a] Oliver.[3]

5. Sellei, J.: Weitere Beiträge zur Fermenttherapie des Skleroderma, Arch. f. Dermat. u. Syph. **171**:577, 1935.

ferment-producing organs, principally the pancreas, as etiologic agents in scleroderma and sclerodactylia and has advocated the administration of pancreatic, duodenal and gastric ferments for the relief of the vascular spasm, especially when associated with sclerodactylia (acrosclerosis). The presence of arteriosclerosis and of arteriosclerosis obliterans with intermittent claudication in scleroderma has received little or no attention in the literature, and I was unable to find any reference to intermittent claudication associated with scleroderma and sclerodactylia. It is believed, therefore, that the following report of a case will be of interest.

REPORT OF A CASE

C. B. W., a married man aged 58, consulted me on June 3, 1936, for ulcers on the tips of the right index and middle fingers. He had enjoyed fairly good health for a number of years. He had lived in the tropics during the past fifteen years, having spent the greater part of this time in Manila, P. I. A prostatectomy had been performed in 1935. The patient had made a good recovery from this. He had been an extremely heavy smoker for the greater part of his life, consuming from twenty-five to thirty-five cigarets per day. Recently slight nasal hemorrhages had occurred several times a month.

About ten years before, the patient had noticed that the feet and the tips of the fingers of both hands felt cold. Small calluses had developed at the ends of the fingers and had disappeared after a short time. During the past year the skin over the fingers had become thickened, hard to the touch, rigid and bluish white. About six weeks previous to consultation the patient had filed the ends of several finger-nails on the right hand, and infection had followed in the index and middle fingers. Under the nail beds of these two fingers there had appeared painful, slow, indolent ulcers, which had refused to heal.

During the past few months the patient had felt severe pain in the lower part of the right leg after walking a short distance. The pain had been so severe that it necessitated immediate cessation of walking. Rest while sitting was necessary before walking could be continued.

The general examination showed absence of pulsations in the right popliteal, posterior tibial and dorsalis pedis arteries and the ulnar arteries at both wrists; marked pallor on elevation of the right foot and rubor on pendency, and systolic and short diastolic murmurs over the entire precordium, with a regular irregularity in rhythm, so that there occurred a dropped beat with every third pulsation. The blood pressure was 145 systolic and 75 diastolic. The neurologic examination indicated complete normality except for the aforementioned vasomotor and trophic disturbances.

The dermatologic examination revealed pathologic changes on the extremities and the face. The skin of the hands and the fingers was white, hard and thick and showed loss of elasticity. It felt tight, leathery and smooth. On the tips of the first, second and third fingers of the right hand beneath the nails were sharply defined deep ulcers. The hands and feet were bluish white and cold on palpation. The skin of the face was smooth and hard. The loss of the normal facial furrows resulted in a masklike appearance. Indurated, thickened areas were present on the feet, the lower parts of the legs and the arms. There was marked hyperhidrosis of both palms. On the face, the forearms, the hands and the fingers were multiple discrete tiny telangiectases.

Laboratory Examinations.—The blood count showed: hemoglobin, 14.9 Gm. per hundred cubic centimeters, and erythrocytes, 4,080,000, and leukocytes, 7,300, per cubic millimeter. The Kolmer and Kahn reactions of the blood serum were negative. The sugar content of the blood was 90 mg. per hundred cubic centimeters. The urinalysis gave negative results except for a moderate amount of pus evident under the microscope.

The roentgen examination of the chest showed calcifications and slight torsion of the aortic arch, no calcification of the arteries of the legs, no abnormality of the cervical portion of the spine and irregularity of the distal phalanges of the first, second and third fingers of the right hand and of the third and fifth fingers of the left.

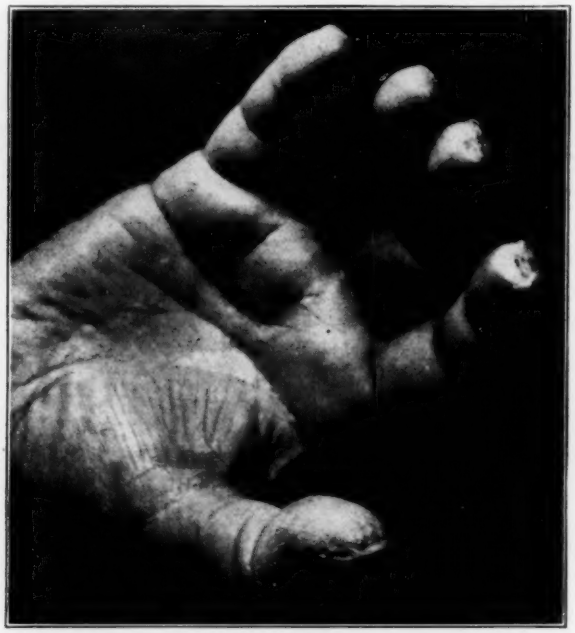

Fig. 1.—Sclerodactylia with trophic ulcers on the tips of the fingers and hard callous formation on the tip of the thumb.

The electrocardiogram showed premature auricular contractions, preponderance of the left ventricle and delayed auriculoventricular conduction. The PR interval was three-tenths second. The basal metabolic rate was —10 per cent.

The vasomotor index with alcohol showed a rise in the left fingers to 35 C. and in the right fingers to 34.5 C. In the toes of the left foot there was a rise to 33 C. and of the right foot to 29 C. Exposure of the hands to heat or immersion in hot water helped to raise the temperature of the surface only temporarily. The time before claudication set in on exercise (walking) was two minutes and forty seconds.

COMMENT

The association of intermittent claudication with scleroderma and sclerodactylia is of interest from the etiologic standpoint and has not heretofore been described. My patient presented evidence of definite occlusive arterial disease of the right leg, as shown by the loss of pulsations in the popliteal, posterior tibial and dorsalis pedis arteries of that side. Pulsations were also absent in the ulnar arteries of both wrists. The pallor on elevation of the right foot, followed by rubor on dependency, and the lowered vasomotor index of the toes of the right foot, together with the claudication after exercise, tend to confirm the suspicion of such occlusive arterial disease. Telangiectasia, calcification of the aortic arch and cardiac disturbance were also noted. Arteriosclerosis obliterans was probably the etiologic basis for the intermittent claudication.

Scleroderma and sclerodactylia have been generally considered to be angiotrophoneurotic disorders. The question arises as to the relation in my case between the arteriosclerosis obliterans with claudication and the sclerodermic and sclerodactylic changes. My patient probably presented two separate conditions: the scleroderma with vasospastic disturbance of the fingers and trophic ulcers and arteriosclerosis obliterans of the right leg, with claudication.

At the present time the patient is receiving intramuscular injections of 0.75 cc. of solution of posterior pituitary of double U. S. P. strength daily and 3 cc. of an insulin-free extract of pancreas hypodermically twice a week. Under this therapy it is of interest to note that the claudication time has increased from two minutes and forty seconds to six minutes. The skin on the hands and the face is less stiff, and the ulcers of the fingers have healed.

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AINHUM

REPORT OF SIX CASES IN NEW YORK

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The name ainhum is described in "Manson's Tropical Medicine" as being derived from the Nago dialect, meaning "to saw or cut."

The condition consists in the formation of a constricting ring involving a part of or the entire circumference of the fifth toe, at or near its base. This furrow deepens, eventual spontaneous amputation of the portion distal to the constriction resulting.

REVIEW OF THE LITERATURE

Ainhum was described clinically by Clark in 1860 as occurring in natives of the African gold coast, but the name ainhum was introduced in 1867 by da Silva Lima.

The majority of cases are reported from Africa, India and Brazil (Crawford, Duhring, Pyle, Matas, Herrick, Abbe). Although the disease occurs most frequently in African Negroes and Hindus, cases have been recorded in Arabs and Chinese.

It is of rare occurrence in the white race; cases have been reported by Aubry, De Brun, Castellani, Hyde and Montgomery from Algeria, Syria and southern Italy; by Nielly, Coni, Gougerot, Sézary and Gallot from Senegal and North Caledonia; by Zambaco Pacha and Duhring from Istanbul; by Pineaux, Legroux and Lancereaux from different parts of Europe; by Pospelow and Grschebin from Russia; by Zavattari from Libya, and by Onorato and Giordano from Tripoli.

Until 1911 only thirty cases had been reported in the literature from the United States; all had occurred in Negroes from the Gulf states and from North and South Carolina. More recently, Friedman, Bloom and Newman, and Irgang and Alexander each reported one case of ainhum occurring in Negroes residing in New York who had migrated from the southern states. Probstein's case was that of a Missouri Negro who had migrated from Mississippi.

From the Outpatient Department, Hospital for Joint Diseases.

CLINICAL PICTURE

As stated, the constricting ring involving the circumference of a toe, usually the fifth, deepens and frequently causes spontaneous amputation through the second or third joint or through the phalanx. The distal portion prior to its severance becomes bulbous and hypertrophied. Progress of the constriction may cease at any point.

The groove is usually located over the first interphalangeal joint; the next most frequent location is over the second phalanx, the depression commencing on any surface. The little toe is most frequently involved, and the involvement is usually symmetrical, but any or all of the toes may be similarly involved, the fourth being affected in 10 per cent of the cases (da Silva Lima).

The disease usually affects men from 20 to 40, but occasionally children or women suffer from it. Patients with ainhum are often in otherwise perfect health.

The Wassermann reaction may be positive, as in one of our cases, but antisyphilitic therapy has no specific effect on the course of the disease, although iodides, given intravenously and orally, have been used successfully to relieve the pain. Pain is present when ulceration takes place. In many cases the enlarged distal portion of the toe, attached by a pedicle, causes discomfort to the patient on motion.

Sensation of the affected toe is diminished or increased but not lost. The plantar reflexes may be absent, but there are no other definite neurologic findings.

Ainhum is frequently familial in occurrence; in 50 per cent of Maass' cases there was a history of familial predisposition, while da Silva Lima described the occurrence of the disease in an entire family of Negroes.

ETIOLOGY

The process is probably a mechanical one produced by a fibrotic constriction which is induced by mechanical or infectious injury. Many observers (Facio, Manson, Eyles) have ascribed it to chronic irritation. Matas, Abbe, Weinstein and others considered it as a trophoneurosis. Castellani and Pusey sought a parasitic cause, while Le Brun classed it among the neuritides.

A few observers (Zambaco Pacha, Pardo-Castelló and Mestre and Harrower) stressed its similarity to leprosy, while others noted its close association with keratoderma and scleroderma (Kaposi, Besmier, Pospelow). Grschebin reported a case in which combined icthyosis and keratoderma palmare and plantare of seventeen years' duration were followed by typical ainhum of both fifth toes.

Certainly in trophoneuroses such as sclerodactyly, keratoderma and the anesthetic type of leprosy all the necessary conditions are present

for the development of ainhum, which the aforementioned authors consider as a symptom rather than as an independent disease.

PATHOLOGY

Studies by Wucherer, Schüppel, Duhring, Eyles, Unna, Weinstein and Castellani indicate that the tissues beneath the constricting ring show more or less atrophy and that the bone evidences rarefying changes and ultimately fragmentation and absorption.

Endarteritis and periarteritis of the vessels occur distal to the band, with atrophy of the part proximal to the ring and fatty degeneration

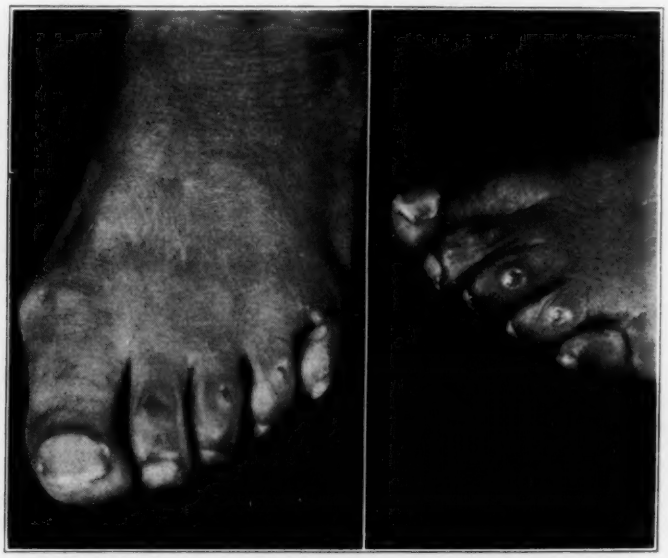

Fig. 1.—Photographs showing constricting band involving the soft tissues of the fifth toe.

and edema of the distal bulbous portion. Separation occurs through the shaft of the base or through an interphalangeal joint.

ROENTGENOGRAPHIC FINDINGS

Constriction of the soft tissues of the toe, especially of the fifth, is highly suggestive of ainhum. There is secondary narrowing of the shaft of the underlying phalanx with rarefaction, fragmentation and absorption of its distal portion.

In Raynaud's disease, leprosy and thrombo-angiitis obliterans, several toes of the same foot are involved simultaneously, showing marked atrophy and destruction of the distal phalanges and absence of the constricting band.

TREATMENT

If symptoms are mild, one may assume a passive attitude and await spontaneous amputation.

Most authors agree that ablation of the toe or removal of the distal part is advisable when uncontrollable pain is present. Perpendicular

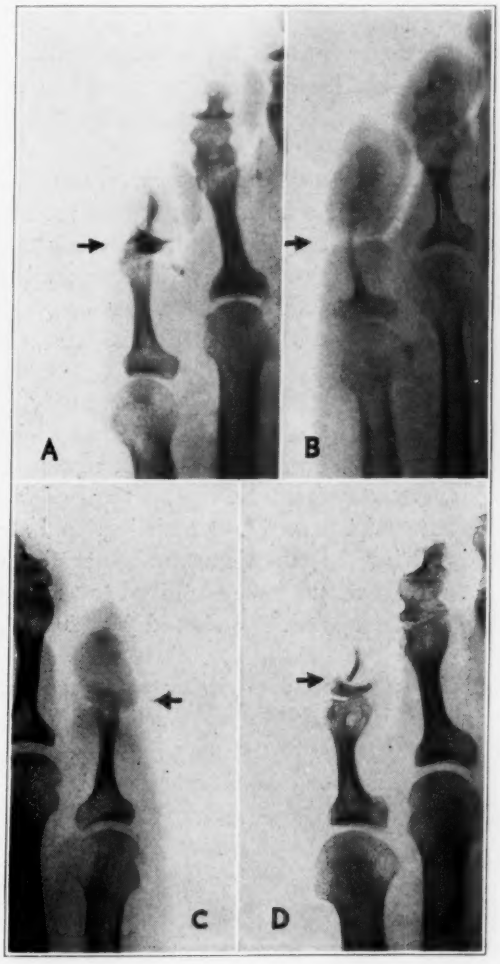

Fig. 2.—Roentgenograms showing osseous changes in patients with ainhum affecting the fifth toe. *A*, left fifth toe of a man aged 40; *B*, left fifth toe of a woman aged 41; *C*, right foot of a man aged 40; *D*, left foot of a man aged 47.

incision of the band as advocated by da Silva Lima has not proved uniformly beneficial.

Antisyphilitic therapy does not alter the course of the disease, but oral or intravenous administration of iodides may successfully be

employed to control intractable pain in patients who refuse to undergo surgical treatment (Irgang and Alexander).

REPORT OF CASES

In this series of six patients, all of whom were Negroes living in the Harlem section of New York, there were four men and two women, ranging in age from 40 to 47. One had originally migrated from the British West Indies; the remainder had come from the southern states.

In all the patients only the fifth toe was involved; the involvement was unilateral in five cases, the right foot being affected in three and the left in two, and bilateral in one.

No definite history of direct trauma was obtained. Only two of the patients complained of pain in the involved toe; it was unassociated with ulceration and readily controlled with anesthetic ointments.

The Wassermann reaction of the blood of one patient was positive, but despite vigorous antisyphilitic therapy, the constriction advanced steadily. Studies for fungous infection gave consistently negative results.

Follow-up was largely by correspondence, as only one of the six patients attended the clinic regularly. In none has spontaneous amputation occurred over a period varying from six months to three years.

No histologic studies were made.

Clinically the patients presented a constricting band of varying depth and magnitude, involving the soft tissues at the middle or base of the fifth toe (fig. 1). The portion of the toe distal to the constricting band was bulbous and hypertrophied, the skin dry and thickened and the nail atrophic.

Roentgen studies revealed constricting and rarefying changes of varying intensity in the phalanx, with ultimate fragmentation and absorption. The constriction of the adjacent soft tissues of the toe, present in all cases, is of diagnostic significance (fig. 2).

CONCLUSION

Six cases of ainhum, commonly considered a tropical disease, are reported from New York. The occurrence of this condition must be anticipated especially in Negroes, irrespective of geographic location.

BIBLIOGRAPHY

Abbe, T.: Two Cases of Ainhum, M. Rec. **79**:478, 1911.

Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930.

Aubry, G.: Un cas d'aïnhum chez un European, Bull. et mém. Soc. méd. d. hôp. de Paris **54**:1361 (July 21) 1930.

Bharucha, E. S.: Notes on a Case of Ainhum, Indian M. Gaz. **52**:403, 1917.
Bloom, D., and Newman, B.: Ainhum: Report of a Case with Roentgenologic Findings and a Review of the Literature, Arch. Dermat. & Syph. **27**:783 (May) 1933.
Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, ed. 3, New York, William Wood & Company, 1919.
Clark: Tr. Epidemiol. Soc., London **1**:105, 1860; cited by Bloom and Newman.
Crawford, D. G.: Notes on Four Cases of Ainhum, Edinburgh M. J. **31**:1120, 1885, 1886.
Da Silva Lima, J. F.: On Ainhum, Arch. Dermat. **6**:367, 1880.
Dschang, Y. D.: Beitrag zur pathologischen Anatomie des Ainhum, Virchows Arch. f. path. Anat. **290**:648, 1933.
Duhring, L. A.: A Case of Ainhum, Am. J. M. Sc. **87**:150, 1884.
Eyles, C. H.: The Histology of Ainhum, Lancet **2**:576, 1886.
Facio, A. A.: A Review of Ainhum, with Radiographic Demonstration of Its Bone Pathology, Proc. Internat. Conf. Health Prob. Trop. Am. **1**:533, 1925.
Friedman, L. J.: Roentgen Findings in Ainhum, Am. J. Roentgenol. **31**:349, 1934.
Giordano, M.: Un caso di ainhum in Tripolitania, Ann. di med. nav. e colon. **40**: 529, 1934.
Grschebin, S.: Observations on Ainhum: Does It Exist as an Independent Disease? Urol. & Cutan. Rev. **40**:98, 1936.
Harrower, G.: Ainhum Disease and an Anesthetic Type of Leprosy, Tr. Roy. Soc. Trop. Med. & Hyg. **29**:73, 1935.
Herrick, J. B.: A Case of Ainhum, Philadelphia M. J. **1**:246, 1898.
Hornady, E. H.: Ainhum, North Carolina M. J. **8**:116, 1881.
Irgang, S., and Alexander, E. R.: Iodide Therapy for Relief of Pain in Ainhum: Report of a Case, Arch. Dermat. & Syph. **30**:508 (Oct.) 1934.
Maass, E.: Beobachtungen über Ainhum, Arch. f. Schiffs- u. Tropen-Hyg. **30**:32, 1926.
Onorato, R.: L'ainhum, Arch. ital. di sc. med. colon. **1**:268, 1920.
Pardo-Castelló, V., and Mestre, J. J., cited by Grschebin.
Pawlowskaja-Karyschewa, cited by Grschebin.
Probstein, J. G.: Ainhum, Ann. Surg. **88**:885, 1928.
Pyle, W. L.: Ainhum, M. News **66**:85, 1895.
Schüppel, F. J.: Postscript to article by Wucherer, p. 381.
Sézary, A., and Gallot, H.: Ainhum, Bull. Soc. franç. de dermat. et syph. **40**:566, 1933.
Stelwagon, H. W.: Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1921.
Stitt, E. R.: Diagnosis and Treatment of Tropical Diseases, ed. 5, Philadelphia, P. Blakiston's Son & Co., 1929.
Weinstein, H.: A Description of Ainhum, with Report of Interesting Cases Occurring in One Family, Proc. Canal Zone M. A. **4**:110, 1911.
A Description of Ainhum, South. M. J. **6**:651, 1913.
Welch, R. S. G.: Ainhum, U. S. Nav. M. Bull. **21**:352, 1924.
Wigley, J. E. M.: A Case of Hyperkeratosis Palmaris and Plantaris Associated with Ainhum-Like Constriction of the Fingers, Brit. J. Dermat. **41**:188, 1929.
Wucherer, O.: Ueber Ainhum, eine der afrikanischen Rasse eigenthümliche Krankheitsform, Virchows Arch. f. path. Anat. **56**:374, 1872.
Zavattari, E.: L'ainhum mel Fezzan, Arch. ital. di dermat., sif. **10**:343, 1934.

BORIC ACID-STARCH POULTICE

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I first became aware of the starch poultice through Sabouraud [1] and of the addition of boric acid to it through Macleod,[2] who, possibly from an appreciation of its value, has placed directions for making it at the head of his list of remedies.

In prelisterian medicine the poultice occupied a too prominent place, and its subsequent neglect has been partly a reversion from this excess. One of the chief reasons, however, why the poultice has fallen into desuetude is undoubtedly the dirty appearance and messiness of the linseed poultice, for cleanliness has now become a cult. The starch poultice, however, when well made, is a clean-looking white jelly, not repugnant to the tidiest nurse.

The old-fashioned linseed poultice had excellent qualities, some of which were not mentioned in books on therapeutics. When the condition of the patient is grave, for example, persons often crowd around the physician and patient, lamenting and asking inane questions, just as cows crowd around a wounded member of the herd, lowing all the while. At such a time the patient's solicitous friends may be cleared from the room by the simple expedient of ordering the preparation of a poultice.

The following incident illustrates the value of this maneuver in securing quiet and rest and also exhibits another excellent quality of the remedy, the conveyance of bland, relaxing warmth. Years ago I was called at night to see a young druggist's clerk who had employed a strong ointment containing menthol for epididymitis. The salve caused extreme contraction and deep wrinkling of the scrotum, and unfortunately the preparation was caught in the depths of the wrinkles. The pain from the menthol was agonizing, and it was hopeless to try to remove the ointment while the contraction continued. The preparation of a poultice dispelled the sympathetic audience, and its application was shortly followed by relaxation of the scrotum, so that the diluted salve could be wiped easily from the smooth surface. I have rarely received an expression of deeper gratitude than I did from this patient.

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1. Sabouraud, R.: Le cataplasme de fécule en dermatologie, in Entretiens dermatologiques, Paris, Masson & Cie, 1913, p. 415.

2. Macleod, J. M. H.: The Boro-Starch Poultice, in Diseases of the Skin, New York, Paul B. Hoeber, Inc., 1921, p. 1267.

Another instance relates to a much deeper involvement. Inflammation of the gasserian ganglion causes some of the severest, most dangerous forms of herpes zoster. In a case in which such a condition was accompanied with severe neuralgia and a very extensive eruption, I first gave the patient half an erythema dose of roentgen radiation over the gasserian ganglion and then ordered him to bed immediately. I instructed him to apply a boric acid-starch poultice over the entire vesicular surface and to take a teaspoonful of camphorated tincture of opium every hour until the pain abated. He made a quick and comfortable recovery, and the celerity with which the eruption disappeared was astonishing. I am inclined to give more credit for the fortunate outcome to the confinement in bed, the camphorated tincture of opium and the poultice than to the roentgen radiation.

To digress for a moment: J. E. Graham, one of the earliest members of the American Dermatological Association, used often to say that he thought opium had a direct effect in diminishing acute inflammation, and many of his contemporaries were of the same opinion. Furthermore, the man who first added camphor to this beneficent but now much neglected drug, making the camphorated tincture, had a keen therapeutic sense.

In such vesicular, crusted eruptions as the one described—and there are many of them in dermatologic practice—the hydrated starch absorbs the moisture, softens the crusts and allows the gently astringent antiseptic, boric acid, to come into immediate contact with the denuded surface without being in the least irritating.

The composition of the linseed poultice was a simple matter. Some linseed meal and hot water and cheese-cloth or muslin in which to wrap it were the only requirements.

But in the composition of a boric acid-starch poultice details must be respected, or instead of a jelly a disagreeable lumpy mess will be produced. The following is the best procedure: Mix together in a small dish 1 tablespoonful of ordinary laundry starch powder and 1 heaping tablespoonful of boric acid powder. Make a paste by adding 2 tablespoonfuls of cold water. Then add to this paste, while constantly stirring, half a standard measuring cupful of boiling water. The quantity of water is important, and it must be boiling for proper hydrolysis. In measuring the starch, use as nearly a level tablespoonful as possible; the starch being in lumps, it is impossible to make the amount absolutely exact. There are many kinds of starch, but, as they do not hydrolyze alike, not all of them make good poultices. A starch made from corn is excellent for this purpose. Well hydrolyzed starch jells excellently and may be applied warm or cold.

Typed, printed or written directions for preparing the poultice should be given to the patient. Patients are neither doctors nor nurses, and they become confused in the simplest matters.

There is another detail: After the poultice has been in place for some time, the edges, if exposed, may dry and stick disagreeably to the skin. To avert this the under-margins of the poultice may be smeared with simple ointment or with olive oil. Cellophane or oiled silk may be employed to enclose the poultice. To prevent the poultice from drying too fast one may add a little glycerin [3] to the water used in making it.

Poultices have been made of all sorts of materials: A popular one is made of kaolin, and a very good one, requiring little skill, may be made of bread, to which may be added boric acid as in the case of the starch poultice.

Making a poultice may not be a lofty occupation, but one must remember, as a well known physician once remarked, that where the patient is concerned there are no small things.

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3. Brocq, L.: Précis-atlas de pratique dermatologique, Paris, G. Doin, 1921, p. 69.

ECTODERMOSIS EROSIVA PLURIORIFICIALIS

ITS RESEMBLANCE TO THE HUMAN FORM OF FOOT AND MOUTH DISEASE AND ITS RELATION TO ERYTHEMA EXSUDATIVUM MULTIFORME

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Rendu [1] and later Fiessinger and Rendu,[2] French military surgeons, reported what they believed to be a new infection. It was subsequently named ectodermosis erosiva pluriorificialis.

The disease is characterized by an acute onset with fever and constitutional symptoms and a vesicular eruption involving notably the hands and feet, accompanied by an inflammation of some or all of the orifices—mouth, nose, conjunctiva, urethra, vagina and anus.

Some writers, notably the French, regard the disease as a clinical entity, whereas others believe it is one form of erythema exsudativum multiforme. Cases of ectodermosis erosiva pluriorificialis are herein reported—the first to be recorded under this name in English. The resemblance of the condition to the human form of foot and mouth disease is later discussed, as well as the different forms of erythema multiforme, of which ectodermosis erosiva pluriorificialis is regarded as one.

SYMPTOMS AND COURSE OF ECTODERMOSIS EROSIVA PLURIORIFICIALIS

The disease occurs most frequently in young men and between February and June. The onset is acute, with a temperature of from 102 to 104 F. and with constitutional symptoms, headache, chill, malaise and soreness of the throat and mouth. Stomatitis is an early and conspicuous symptom. At the onset vesicles are present on the inner surfaces of the lips, the tongue and the buccal mucosa. Later the picture is that of a severe and extensive stomatitis, with a pseudomembrane which bleeds easily when removed. Ulcerations may or may not occur. Inflammation involves the throat and may extend to the epiglottis. There is

1. Rendu, R.: Sur un syndrome caracterisé par l'inflammation simultanée de toutes les muqueuses externes coexistant avec une éruption varicelliforme puis purpurique des quatre membres, Rev. gén. de clin. et de thérap. **30**:351, 1916.

2. Fiessinger, N., and Rendu, R.: Sur un syndrome caraterisé par l'inflammation simultanée de toutes les muqueuses externes coexistant avec une éruption vésiculeuse des quatre membres, non douloureuse et non récidivante, Paris méd. **23**:54, 1917.

profuse salivation, and eating and drinking become difficult. There is invariably a bilateral conjunctivitis of variable degree, at the onset of which vesicles may be seen. Rhinitis may occur, in which event the nares are covered with crusts and there is epistaxis. Involvement of the genitalia is common and is seen as balanitis, with vesicles involving the glans penis, the meatus especially, and less commonly the scrotum. Ulcers were present on the vulva and in the vagina in the case reported by Schreuder.[3] Urethritis may occur. Occasionally the anus and the perianal region are involved, with redness, vesicles or superficial ulcerations.

A few days after the onset an eruption appears, which favors the hands and feet. The following forms have been reported for this eruption: bright red spots, purpuric lesions, vesicles resembling vari-

Fig. 1 (case 1).—Ectodermosis erosiva pluriorificialis (erythema multiforme) showing rhinitis, conjunctivitis and involvement of the lips as part of stomatitis.

cella with erythematous or purpuric halos, grouped vesicles resembling herpes, papules covered with blackish crusts, erythematous lesions with central vesicles resembling erythema multiforme and vesicles which undergo involution with crusting and in which a collar of scale remains around the congestive residue when the crust falls off. Although the eruption favors the hands and feet, scattered lesions at times appear on one or more of the extremities. A few cases have been reported in which there were no cutaneous lesions, the patient presenting stomatitis, rhinitis and conjunctivitis. Such an instance is seen in figure 1. Some writers regard this as one of the varieties of the disease.

The lymph nodes are usually not enlarged. If enlargement is present, it is slight.

3. Schreuder, J. J. C.: Een beval von ectodermosis erosiva pluri-orificialis bij eene vrouw, Nederl. tijdschr. v. geneesk. **1**:874 (Feb. 27) 1926.

Cultures of the blood have given negative results. Bacteriologic studies of secretions from the mouth and the conjunctiva and inoculations of animals with such secretions and the content of vesicles have furnished no clue as to the cause of the disease. There is usually albuminuria. The condition of the blood is generally not changed. Exceptions were the case reported by Fiessinger and Rendu,[2] in which leukopenia was present, and the case reported by Fiessinger, Wolff and Thévenard,[4] in which there was a high leukocyte count, with mononucleosis.

The temperature is usually high and slowly becomes normal. The course of the disease is from three to six weeks. Cutaneous lesions and conjunctivitis are the first symptoms to disappear. The lesions of the mouth and throat may persist in an attenuated form for some weeks after all other symptoms have disappeared. In a few of the reported cases relapse occurred.

Fig. 2 (case 2).—Ectodermosis erosiva pluriorificialis (erythema multiforme) showing vesicles on the tongue.

Case 1.—A Negro boy aged 7 years complained of sore mouth, nasal discharge, inflamed eyes and fever one week prior to admission to the hospital. There was moderate stomatitis. The lips were swollen, red and partly covered with crusts. The nasal mucosa was inflamed, and there was free secretion, which formed crusts on the nares and upper lip. There was a pronounced inflammation of the palpebral and bulbar conjunctivae with a seropurulent discharge. There were no cutaneous lesions. During ten days' stay in the hospital the patient's temperature was about 101 F. for the first seven days.

The following case and figures 2 and 3 are those of another boy with ectodermosis erosiva pluriorificialis. The clinical picture closely resembled the human form of foot and mouth disease.

4. Fiessinger, N.; Wolff, M., and Thévenard, A.: Ectodermose erosive pluriorificielle, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:446, 1923.

CASE 2.—*History.*—A boy aged 13 was admitted to the Delaware County Hospital, Drexel Hill, Pa., service of Dr. H. S. Busler, on July 2, 1935. One week prior to admission he had a "cold in the chest," felt generally ill and suffered from anorexia, malaise and headache. He was nauseated, vomited and was constipated. He complained of a sore mouth and throat. He was well prior to the onset of this illness.

Examination.—On admission he appeared ill. The temperature taken by rectum was 104 F. There was bilateral conjunctivitis, with seropurulent discharge. There was no rhinitis. The lips were inflamed and partly covered with crusts. The tongue was coated and in its center there were a number of tense vesicles of various sizes (fig. 2). Vesicles were present on both sides of the buccal mucosa, the soft palate and the pharynx. In addition there were irregular patches covered

Fig. 3 (case 2).—Ectodermosis erosiva pleuriorificialis (erythema multiforme) showing inflamed lips as part of stomatitis, conjunctivitis and vesicles on palms and fingers. There was a similar eruption on the soles. The clinical picture resembled the human form of foot and mouth disease.

with moist white membrane on the buccal mucosa, the gums and the anterior pillars of the tonsils. The soft palate, the uvula, the anterior pillars of the tonsils and the pharynx were red and edematous. The anterior cervical lymph nodes were moderately enlarged. The lungs were resonant, sibilant râles being heard throughout both.

Two days after the patient's admission, a vesicular eruption appeared on both palms and the palmar and lateral surfaces of the fingers (fig. 3). Some vesicles had purplish red halos. A few bullae were present. In addition, there were purpuric spots about the size of a split pea. The soles presented a similar eruption. The dorsal surfaces of the hands and feet were free. There were a few vesicles on the dorsal surfaces of both wrists and a few vesicular lesions without halos of

inflammation on the forearms and thighs. The foreskin was adherent to the glans, and apparently balanitis was present. A few vesicles on the foreskin and on the meatus interfered with urination.

The human form of foot and mouth disease was considered in diagnosis. There was no history of exposure to this infection. Veterinarians informed me that the disease was not reported in cattle in Pennsylvania or nearby states; nevertheless, guinea-pigs were inoculated in an effort to demonstrate the virus of foot and mouth disease.

Laboratory Examination.—Serum obtained from vesicles was placed on scarified areas on the plantar surfaces of the feet of guinea-pigs (Waldmann and Pape's method). The result was negative. The urinalysis and the Wassermann test gave negative results. The blood count showed 5,550,000 red cells and 14,800 white cells, with 76 per cent neutrophils. Examination of smears from the mouth and throat did not show Vincent's organism. Cultures of material from the mouth and throat showed mostly Streptococcus viridans and Micrococcus catarrhalis, and cultures of material from the conjunctivae showed Staphylococcus aureus. Culture of the blood showed no growth.

Course.—A few days after the patient was admitted, vesicles on the tongue and in the mouth disappeared. Inflamed patches involving the buccal mucosa became confluent, presenting the appearance of a severe stomatitis. Ulceration did not occur. Eating and drinking were difficult. Mucopurulent expectoration tinged with blood suggested involvement of the larynx and the bronchi. The cutaneous lesions began to disappear five days after their onset. The temperature ranged from 100 to 104 F. for six days and gradually became normal two weeks after admission. The stomatitis was much improved one week after admission. Attenuated areas of stomatitis were present at the time of discharge, twenty-four days after admission, and did not completely disappear until two months after their onset.

About twenty reports have appeared in the literature concerning ectodermosis erosiva pluriorificialis. In addition to those already quoted, mention may be made of the papers by the following authors: Jausion and Diot,[5] Aubert,[6] de Lavergne,[7] Chantegreil[8] and Kumer.[9]

5. Jausion, M. H., and Diot: Sur les rapports de l'ectodermose érosive pluriorificielle de Fiessinger, Wolff et Thévenard avec l'hydroa vésiculeux de Bazin, Ann. de dermat. et syph. **6**:440, 1925.

6. Aubert, M.: Observations sur quatre cas d'ectodermose érosive, Arch. de méd. et pharm. mil. **98**:155, 1933.

7. de Lavergne: A propos de la communication de M. M. Fiessinger, Wolff et Thévenard sur l'ectodermose érosive pluriorificielle, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:462, 1923.

8. Chantegreil, B.: Sur un cas d'ectodermose érosive pluriorificielle et périorificielle chez un Sénégalais, Arch. de méd. et pharm. mil. **101**:397, 1934.

9. Kumer, L.: Ectodermose érosive pluriorificielle und Erythema exsudativum multiforme, Dermat. Ztschr. **72**:62, 1935.

ECTODERMOSIS EROSIVA PLURIORIFICIALIS AND THE HUMAN FORM OF FOOT AND MOUTH DISEASE

Ectodermosis erosiva pluriorificialis resembles the human form of foot and mouth disease, from which it should be differentiated. It should be recalled that conjunctivitis, rhinitis and balanitis may be present in the human form of foot and mouth disease. Distinctive features which differentiate the condition from ectodermosis erosiva pluriorificialis are: considerable burning and dryness in the mouth, inflammation, redness and swelling around the nails of the hands and feet and desquamation, usually occurring at the sites of vesicles on the fingers and toes.

In some established cases of foot and mouth disease there were oral lesions without accompanying cutaneous lesions, and in still others cutaneous lesions appeared without accompanying oral lesions.

Proof in the laboratory of the presence of the disease was not possible until 1920, when Waldmann and Pape demonstrated the virus by inoculation of guinea-pigs (see laboratory examination in case 2). It is likely that some of the conditions reported as the human form of foot and mouth disease with bizarre eruptions—disseminated vesicles, macules, papules, papulopustules and hemorrhagic macules—in which animals were not inoculated were erythema multiforme of the type of ectodermosis erosiva pluriorficialis.

ERYTHEMA EXSUDATIVUM MULTIFORME: ITS VARIABLE CLINICAL PICTURE

French writers champion the view that ectodermosis erosiva pluriorificialis is an entity and not a form of erythema multiforme. In view of this, it becomes pertinent to discuss what constitutes erythema multiforme and its symptom complex. Hebra in 1866 separated from the heterogeneous group of polymorphous erythemas a syndrome which he regarded as a clinical entity and which he called erythema exsudativum multiforme. The cutaneous lesions described were dark blue or purplish erythematous lesions of variable shape, papular and nodular lesions, erythema iris and herpes iris.

Hebra stressed the invariable location of the eruption on the dorsa of the hands and feet. When severe it was present on the arms and legs and in exceptional cases on the trunk and the face or on the entire cutaneous surface. Other salient features in Hebra's description were fever, constitutional symptoms, occurrence of the disease in April, May, October and November and a tendency to relapse.

Subsequent observation has served to complete Hebra's description by adding additional symptoms and forms of the disease, as shown in the following discussion and in the table. Erythema multiforme may

involve the skin alone, the mucous membranes alone, or the skin and the oral, nasal, ocular, genital, anal, tonsillar, uvular, pharyngeal and laryngeal mucous membranes. The cutaneous lesions are well known and need not be discussed. The most distinctive lesions are annular ones with central clearing (target shaped), erythema iris and herpes iris. Hemorrhagic macules and crusts and scales are rare.

The palmar surfaces, rather than the dorsal surfaces, of the hands and feet may be involved; the most distinctive lesions of the disease may be absent, an example of this being ectodermosis erosiva pluriori-

Scope of Erythema Exsudativum Multiforme

Erythema Exsudativum Multiforme (Hebra) (Probably a specific disease, relapsing, involving skin and mucous membranes. Cutaneous lesions: erythema of variable shape, papules, nodules, vesicles, bullae and hemorrhagic macules. Distinctive lesions: annular erythema with central clearing, erythema iris and herpes iris)						Toxic Erythema Resembling Erythema Exsudativum Multiforme (A cutaneous reaction to various causes. Cutaneous lesions: erythema, vesicles, bullae, angioneurotic edema, urticaria and purpura)
	Types Affecting the Mucous Membranes					
Hebra Type	Ocular	Nasal	Oral	Pluriorificial (Ectodermosis Erosiva pleuriorificialis)	Severe Type (Stevens-Johnson)	
Most common Eruption favors areas of predilection With or without constitutional symptoms or involvement of mucous membrane	Vesicles Simple inflammation Membranous conjunctivitis	Simple inflammation	Vesicles Erosions Diffuse stomatitis	Fever, constitutional symptoms, vesicular eruption on hands and feet, conjunctivitis, stomatitis and rhinitis	Fever, constitutional symptoms Hemorrhagic macules, crusting, scaling, stomatitis, membranous conjunctivitis Leukopenia	Systemic infection Drug eruptions Serum sickness Associated with visceral disease 1. Osler's erythema group 2. Libman-Sacks syndrome Simulating acute lupus erythematosus Toxic erythema described as: 1. Urticaria perstans annulata et gyrata 2. Erythema multiforme perstans 3. Erythema urticatum 4. Erythema bullosum

ficialis. The cutaneous disease with or without involvement of mucous membranes or constitutional symptoms including rheumatoid pains need only be mentioned. Severe forms of erythema multiforme will be discussed later.

Involvement of the mouth may be mild or severe. The severe form is seen as a diffuse stomatitis which may ulcerate and, indeed, develop into gangrene. In cases showing only involvement of mucous membranes the diagnosis of erythema multiforme is presumptive. In such cases, however, cutaneous lesions characteristic of erythema multiforme appear later in the course of the disease, or only in certain relapses. This is illustrated in case 3.

CASE 3.—A woman aged 26 complained of recurring ulcers in the mouth of five years' duration. For about one year the ulcers had recurred at frequent intervals. The first attack, however, had occurred about seven years previously. In my observation over four years, there occurred at intervals of from three to five weeks eruptions of small superficial ulcers ranging in number from three to ten. The surfaces of these ulcers were yellow and red halos were present. The ulcers were tender and painful. They appeared at different sites on the buccal mucosa, the sides of the tongue, the inner surfaces of the lips and the anterior pillars of the fauces. The vagina was never involved. On two occasions only, typical lesions of erythema multiforme appeared on the palms and soles.

Case 4 concerns a patient with recurring severe ulcerative stomatitis and fever. During eighteen months' observation, cutaneous lesions of erythema multiforme did not appear. The diagnosis of erythema multiforme in this case is presumptive.

CASE 4.—*History.*—A man aged 32 was admitted to the Abington Memorial Hospital, service of Dr. Fred Smith, on March 28, 1935. Three weeks before he had complained of a sore throat and later of a sore mouth. Eating was difficult, and pain in the throat interfered with sleep. He had fever.

Examination.—The patient's weight was below normal. The temperature was 103 F. There was extensive stomatitis. Punched-out ulcerations involved both tonsils, the floor of the mouth and the inner surface of the lower lip. Their surfaces were covered with a yellow exudate, which bled easily when removed. A similar ulceration was present on the upper lip at the mucocutaneous junction of the left nostril. The tongue was red and heavily coated. The pharynx was red and congested. There was profuse salivation, and the breath was fetid.

There was no rhinitis, conjunctivitis or cutaneous lesions. The examination otherwise gave essentially negative results.

Laboratory Examination.—A smear of material from the mouth and throat did not show Vincent's organisms. Culture showed Streptococcus viridans. A test of the urine showed considerable albumin. The blood count showed 19,500 leukocytes and 91 per cent neutrophils. The Wassermann test was negative.

Course.—Nasal feeding became necessary. Hemorrhage occurred from the ulceration involving the tonsils. The temperature ranged as high as 103 F., gradually becoming normal about one month after the patient's admission. Improvement was noted ten days after admission and slowly continued. The patient was discharged five weeks after admission. From that time until November 1936 there were frequent recurrences, characterized by the appearance in the mouth of a number of erosive areas coverered with a grayish membrane, and surrounded by a halo of inflammation. At some recurrences erosive lesions appeared on the scrotum. These became superficially ulcerated.

Fuchs [10] described involvement of the conjunctiva [11] in erythema multiforme under the caption "herpes iris conjunctiva." The condition

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10. Fuchs, E.: Herpes iris conjunctivae, Klin. Monatsbl. f. Augenh. **14**:333, 1876.

11. See also Dühring, E.: Beitrag zur Lehre von den polymorphen Erythemen, Arch. f. Dermat. u. Syph. **35**:211, 1896. Hanke, V.: Der Herpes iris des Auges, Arch. f. Ophth. **52**:263, 1901. Bailey, J. H.: Lesions of the Cornea and Conjunctiva in Erythema Exudativum Multiforme (Hebra), Arch. Ophth. **6**:362 (Sept.) 1931.

occurs in a mild and a severe form. The mild form is a simple inflammation. The severe form is characterized by a membranous or aphthous conjunctivitis, which may lead to ulceration of the cornea and subsequent loss of vision. Conjunctival involvement may be the first symptom of erythema multiforme, preceding oral and cutaneous outbreaks. Conjunctival and oral involvement may occur without accompanying cutaneous lesions (fig. 1). This is more likely than the occurrence of conjunctival and cutaneous involvement without accompanying oral lesions. The severe form of conjunctivitis is invariably accompanied with acute constitutional symptoms and pronounced oral and cutaneous symptoms, as shown in the cases reported by Stevens and Johnson. These will be discussed presently.

An instance of a severe and rare form of erythema multiforme, I believe, is represented by the cases reported by Stevens and Johnson [12] as "A New Eruptive Fever Associated with Stomatitis and Ophthalmia." The onset of the disease in two children was that characteristic of an acute infection; among the constitutional symptoms was pain in the joints. An eruption first appeared on the back of the neck and the chest, becoming generalized in about eighteen days. The lesions, at first dark red oval macules, became papular and brownish purple, some acquiring yellow dry necrotic centers. The eruption underwent involution, with crusting and scaling. There was a severe pseudomembranous inflammation of the mucous surfaces of the lip, tongue, mouth, palate, nares, larynx and bronchi. Purulent conjunctivitis was present in both cases. In one, suppurative keratitis ensued, followed by loss of vision. There was leukopenia in one case; in the other case, in which the condition was complicated by pneumonia, the blood count was not reported.

The authors stated that they failed to find reports of a similar condition and mentioned the possibility of a new disease, hitherto undescribed. Somewhat similar cases have been reported subsequently by Rutherford,[13] Wheeler,[14] Bailey [11] and Ginandes.[15] Prominent features of this group of cases are: the likelihood of its occurrence in childhood or early adulthood, the hemorrhagic element of the eruption, suggesting hemorrhagic measles, purulent conjunctivitis with disastrous results to vision, leukopenia and the presence of infections, such as otitis media and pneumonia.

12. Stevens, A. M., and Johnson, F. C.: A New Eruptive Fever Associated with Stomatitis and Ophthalmia, Am. J. Dis. Child. **24**:526 (Dec.) 1922.

13. Rutherford, C. W.: Membranous Conjunctivitis with Loss of Eyeballs: Report of Cases, J. A. M. A. **93**:1779 (Dec. 7) 1929.

14. Wheeler, J. M.: Destructive Purulent Ophthalmia Accompanying an Eruptive Fever with Stomatitis, Tr. Am. Acad. Ophth. **34**:179, 1929.

15. Ginandes, G. J.: Eruptive Fever with Stomatitis and Ophthalmia, Am. J. Dis. Child. **49**:1148 (May) 1935.

The syndrome that is described as ectodermosis erosiva pluriorificialis has long been recognized and has been reported under various names but chiefly as erythema multiforme. I may cite the case of Blair,[16] reported in 1904. The patient was a boy aged 12 years, who had a severe stomatitis and conjunctivitis. Subsequently an erythematous vesicular eruption appeared on the extremities, including the hands and feet. The patient was very ill for two weeks with fever and was prostrated. Recovery ensued in four weeks. There were five subsequent attacks, in one of which there was involvement of the penis and the anus and in another only of the mouth.

The condition described by Baader[17] under the title of dermatostomatitis is somewhat similar to ectodermosis erosiva pluriorificialis and may be regarded as erythema multiforme. Baader's patients had high fever, constitutional symptoms, a severe diphtheroid stomatitis, bilateral conjunctivitis, rhinitis and balanitis. Although the cutaneous lesions resembled erythema multiforme, being composed of bright red papules with a central vesicle or being of the herpes iris type, diagnosis of this disease was not made, since the eruption did not involve areas of predilection of this disease. Inoculation of guinea-pigs to demonstrate the virus of foot and mouth disease gave negative results. In one patient there was a recurrence of stomatitis without cutaneous lesions.

The foregoing cases illustrate the variable picture that erythema multiforme may present and the different names accorded to its variable forms. Besnier and Doyon[18] appropriately wrote:

> Erythema multiforme defies clinical classification; there are an almost infinite variety of clinical symptoms under whose cognomen new forms occur from time to time in the observation of the most experienced clinicians.

In the foregoing passage the term erythema multiforme is used in the sense in which Hebra used it, i. e., a morbid entity which is probably a specific disease. Since Hebra's description appeared many writers have enlarged the scope of erythema multiforme to include erythemas resembling it and occurring under the following circumstances: as an expression of serum sickness or of a drug eruption or as seen in the course of different infections, such as typhoid fever, pneumonia, diphtheria and streptococcic infections, and as associated with visceral disease. The last group includes cases reported notably by Lewin,[19]

16. Blair, L. E.: A Case of Recurring Membranous Stomatitis, Associated with Erythema Exudativum Multiforme (Hebra), M. Rec. **65**:729, 1904.

17. Baader, E.: Dermatostomatitis, Arch. f. Dermat. u. Syph. **149**:261, 1925.

18. Besnier and Doyon, cited by Adamson, H. G.: Discussion on Erythema Multiforme, Brit. J. Dermat. **24**:432, 1912.

19. Lewin, G.: Vorläufige Mitteilung über das Erythema exsudativum, Berl. klin. Wchnschr. **13**:321, 1876.

Galloway [20] and Osler.[21] Symptoms of visceral disease in these cases were endocarditis, pericarditis, arthritis, bronchopneumonia, gastrointestinal dysfunction (notably colic), hematuria and nephritis.

The broad concept of erythema multiforme outlined here envisages the disease as including an idiopathic, or Hebra, type and a symptomatic type occurring under circumstances already discussed.

In this manner erythema multiforme is discussed in most textbooks. Since the cause of the disease is unknown, answers to the question of whether it is a specific disease or a cutaneous reaction to variable causes and of what constitute its scope must remain matters of opinion. One view—the one maintained in this paper—is that it is a specific disease distinct from the other enumerated eruptions resembling erythema multiforme, which are forms of toxic erythema. In this group, lesions that resemble erythema multiforme are erythemas of various shapes, with or without vesicles and bullae. Features that differentiate this group from erythema multiforme are: annular lesions with central clearing (target shape), erythema iris and herpes iris are rare. The erythema is bright red, rather than bluish red. The trunk is more likely to be involved, while the palmar and dorsal surfaces of the hands and feet are less subject to the condition. Urticaria, angioneurotic edema and purpura are present. There is no involvement of the mucous membranes. Recurrences are not characteristic.

As in other diseases of which the etiology is unknown, so with erythema multiforme controversy occurs in classification of allied clinical pictures.[22] Envisaging erythema multiforme as herein reported appears more desirable than giving a new name to what may be regarded as one of the varied forms of erythema multiforme.

1934 Spruce Street.

20. Galloway, J.: Erythemata as Indicators of Disease, Brit. M. J. **2**:121 (July 18) 1903.

21. Osler, W.: On the Visceral Complications of Erythema Exudativum Multiforme, Am. J. M. Sc. **110**:629, 1895; The Visceral Lesions of the Erythema Group, Brit. J. Dermat. **12**:227, 1900; On the Visceral Manifestations of the Erythema Group of Skin Diseases, Am. J. M. Sc. **127**:1, 1904.

22. For example, the clinical manifestations of what are called the lymphoblastoma or the lymphomatoid diseases.

EFFECT OF INFLAMMATION OF THE SKIN ON URINARY EXCRETION OF KETONES

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AND
R. I. KLEIN, M.D.
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In 1935 Midana and del Grande [1] found that extensive inflammation of the skin occurred together with higher levels of ketone bodies in the blood. Not only was the ketonemia found to be greater when ordinary diets were ingested, but ketogenic diets caused more of an increase if a dermatitis was present. Those authors expressed the belief that the inflammation of the skin gave rise to the ketones and that these could not be considered an active causative factor. The skin serves as a storage center for large quantities of glycogen. Midana and del Grande expressed the belief that at the site of inflammation in the skin there is either a lack of normal quantities of available glycogen or interference with its use, causing an incomplete burning of the fats with resultant accumulation of intermediate fat metabolites, the ketone bodies.

Simultaneously, impelled by a different purpose and utilizing another technic, we came to the same conclusions. We were seeking an explanation for the results obtained from the use of maize oil in the treatment of eczema.[2] When a patient takes effective doses of oil he usually markedly cuts down his diet voluntarily. A person on such a restricted diet might conceivably eat such small amounts of carbohydrates as to acquire ketosis. It was therefore natural to investigate this possibility. In making the investigation we selected normal persons as controls and others with various dermatoses for comparison.

The method was that utilized by Behre.[3] In this method, the amount of ketones in a twenty-four hour sample of urine is determined. Behre [4] found that the daily urinary excretion of total acetone bodies is from

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From the Departments of Dermatology and Pathology, University of Illinois College of Medicine.

1. Midana, A., and del Grande, L.: Arch. f. Dermat. u. Syph. **171**:208, 1935.
2. Cornbleet, Theodore: Use of Maize Oil (Unsaturated Fatty Acids) in Treatment of Eczema: Preliminary Report, Arch. Dermat. & Syph. **31**:224 (Feb.) 1935.
3. Behre, J. A., and Benedict, S. R.: J. Biol. Chem. **70**:487, 1926.
4. Behre, J. A.: J. Biol. Chem. **92**:679, 1931.

14.5 mg. to 23.5 mg., or an average of 19.4 mg. The average value for beta-oxybutyric acid was 16.2 mg. and that for acetone 3.2 mg. Our results are shown in the accompanying table.

Our figures for normal subjects compare well with those of Behre and range from 14.6 to 25.9 mg. of total ketone bodies. The excretion for persons with dermatoses was, however, from one and a half to two times as great.

Twenty-Four Hour Urinary Excretion of Ketone Bodies

	Amounts Excreted by Normal Persons			
	Acetone, Mg.	Beta-Oxybutyric Acid, Mg.	Total, Mg.	
1	6.2	16.2	22.4	
2	6.7	10.3	17.0	
3	9.1	10.8	19.9	
4	5.2	9.4	14.6	
5	5.1	15.4	20.5	
6	9.2	16.7	25.9	
7	5.1	11.0	16.1	
8	9.0	15.3	24.3	
	Amounts Excreted by Persons with Various Dermatoses			Type of Dermatitis Present
1	11.2	37.4	48.6	Severe poison ivy dermatitis of the face, extremities and part of the trunk
2	17.3	34.7	52.0	Psoriasis of the trunk and extremities
3	12.5	17.9	30.4	Eczema of the face, neck, upper part of the trunk and flexor areas
4	6.9	20.2	27.1	Erythema multiforme of the face, neck, hands and feet
5	12.3	19.0	31.3	Psoriasis of the elbows, knees, scalp and lower part of the back
6	13.0	29.5	42.5	Exfoliative dermatitis due to arsphenamine
7	9.9	18.7	28.6	Eczema of the face, neck and flexor areas of the extremities
8	6.1	19.2	25.3	Dermatitis venenata of the hands, face and regions about the genitals
9	15.7	23.1	38.8	Severe psoriasis of the trunk and extremities; few patches on the face
10	14.8	29.9	44.7	Severe sunburn; trunk (bathing suit area) spared
11	10.4	22.6	33.0	Psoriasis of the extremities and trunk
12	8.5	18.4	26.9	Eczema of the neck and flexor areas of the extremities
13	13.2	18.0	31.2	Eczema of the face, neck, extremities and upper part of the trunk
14	9.3	27.5	37.8	Pellagra (alcoholic) of the hands, feet and extremities
15	15.0	19.1	34.1	Pemphigus foliaceus

COMMENT

Midana and del Grande made observations on the blood as an index of ketone production. They found that significant changes in dermatoses occurred mostly when their patients were put on a carbohydrate-free diet for twenty-four hours. It appears to us that it would be preferable to determine the urinary excretion of ketone for twenty-four hours, because it is possible for small increases to reflect themselves more decisively by accumulating in a twenty-four-hour sample of urine. The urine collected over such a period gives a composite picture for a span of time, whereas the blood gives but a momentary view of the situation.

When observations are made on the urine, significant changes in the ketones are found in cases of cutaneous inflammation without resort to abnormal diets.

It does not seem to us that the increase in ketone bodies in the urine has a causal connection with the particular types of cutaneous inflammation studied. The changes were found in association with dermatoses of such varied etiology that it is logical to deduce that the increase in ketone bodies was a result of the cutaneous changes.

Just why the cutaneous inflammatory changes should result in an increase of urinary ketones is a matter for speculation. The most attractive possibility would seem to be that inflammation of the skin perverts its normal metabolism. It is known that the skin is an immense reservoir for glycogen. Interference with catabolism of this glycogen could well account for production of ketones, since considerable quantities of sugar need to be burned simultaneously with fat to bring about complete combustion of the latter; otherwise ketone bodies accumulate from the unburned fat.

Another likely possibility is that the accumulation of intermediate fat metabolites results not from perversion of the skin's metabolism but from deficient excretion. Inflammatory states may interfere with sweating. One of us has made observations on sweat production in psoriasis. He was unable to demonstrate any production of sweat in psoriatic patches. If sweat contains any considerable quantities of ketone bodies, these would accumulate in the body when sweating is deficient. If these accumulations were not further broken down, the kidney would be the most likely site for their excretion.

SUMMARY

It was found that there is an increased excretion of ketone bodies in the urine of patients simultaneously with inflammation of the skin. This occurs in association with diverse dermatoses. The amount of increase of these ketones is roughly proportional to the area of skin involved with a dermatitis. The significance of increased ketonuria and modes by which it might possibly be produced are discussed.

DERMATITIS DUE TO JAPANESE LACQUER

REPORT OF A CASE OF INVOLVEMENT OF FIFTEEN YEARS' DURATION

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AND
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PITTSBURGH

It has long been established [1] that Japanese lacquer is a dermal irritant, but it was Pusey's report [2] of a case of lacquer dermatitis, solved through the ingenious work of L. F. Weber, which aroused particular interest in the subject in this country.

Soon after that, Wayson [3] reported cases in canneries, where every can passed through a hot bath of a commercial lacquer and gasoline and often caused papulovesicular dermatitis among the workers.

When the game of mah jong became popular in this country, instances of dermatitis venenata from lacquer on the boxes of mah jong sets were recognized and reported.[4]

The fact that lacquered bowls, plates and cups are in use and that they may be the source of irritation has received little if any attention. The following report of a case illustrates this and also demonstrates the need for better interpretation of cause and effect. The latter is the principal reason for recording this case.

REPORT OF CASE

Mrs. S. M. L., an American housewife aged 42, consulted me on March 6, 1936, for a vesiculo-erythematous eruption which affected her fingers and palms and the flexor surfaces of the wrists. It was of fifteen years' duration. At rare intervals the eruption disappeared for periods not exceeding one or two months.

She had consulted several dermatologists, and eczema, pompholyx, dermatophytosis and neurodermatitis were considered as diagnostic possibilities at various times.

From the Pittsburgh Skin and Cancer Foundation.

1. White, J. C., quoted by Weber, L. F.: External Causes of Dermatitis, Arch. Dermat. & Syph. **35**:145 (Jan.) 1937. Toyama, quoted by Pusey, W. A.[2]

2. Pusey, W. A.: Lacquer Dermatitis, Arch. Dermat. & Syph. **7**:91 (Jan.) 1923.

3. Wayson, J. T.: Lacquer Dermatitis or Dermatosis Industrialis, Arch. Dermat. & Syph. **8**:77 (July) 1923.

4. Levin, O. L.: Dermatitis Venenata from Lacquer on Boxes of Mah Jongg Sets, J. A. M. A. **82**:465 (Feb. 9) 1924. Zeisler, E. P.: Dermatitis Venenata from Lacquer on Boxes of Mah Jongg Sets, ibid. **82**:466 (Feb. 9) 1924.

As a child the patient had had a severe attack of poison ivy dermatitis, and since that time she had remained sensitive to this plant. Her mother and one sister were sufferers from hay fever caused by ragweed and June grass. The same sister was supposedly sensitive to eggs, the ingestion being followed by attacks of eczema.

The patient stated that she looked after her home and performed minor domestic duties, such as dusting, washing dishes and cooking, but no scrubbing or laundry work. She stated emphatically that the eruption was not associated with anything pertaining to these duties. She also did a great deal of knitting and used woolen yarns of various colors. There were plants of all sorts in her home (begonia, English ivy, poinsettia and primrose) which she watered and tended. She owned and bathed two dogs.

She used cosmetics daily and also put perfume on her scalp. She stated that she colored her nails and used removers of nail varnish.

Her hands were more frequently affected in the winter than in the summer, which she spent in a camp, where her occupation was similar to that at home. She stated the belief that her hands improved somewhat when she was in camp, but she was certain that she had had severe attacks there.

The eruption was most annoying when a new attack began, when tiny vesicles arose, the skin became red and hot and the vesicles enlarged somewhat and became firm and tense but did not break spontaneously.

Examination showed that all the fingers, both thumbs, the palms and the flexor surfaces of both wrists were involved in an eruption composed of tiny vesicles, almost confluent, on an acutely inflamed skin. In some areas there were firmly adherent scales. The backs of the hands were unaffected. Between the toes macerated skin and scaling were discernible.

The following factors established by the history and the examination might have played a part in the production of this condition: (1) presence of a bilateral vesiculo-erythematous eruption of fifteen years' duration, remaining localized in special areas on the hands; (2) occasional disappearance of the eruption for periods not exceeding one or two months; (3) lessened severity of attacks in summer; (4) occurrence of the eruption at home and at camp, where the surroundings differed greatly; (5) family history of hay fever and eczema; (6) contact with articles considered as cutaneous irritants, such as house plants, vegetation about camp, cosmetics, colored woolen yarn, dogs, which she washed, and various soaps used in doing housework, and (7) maceration and scaling eruption of the feet, suggestive of dermatophytosis.

Course and Treatment.—Microscopic and cultural examination of the hands and feet and of parings from the nails showed no fungus. Thus, for the time being, dermatophytosis was tentatively excluded.

The patient was instructed to get rid of all her house plants and to stop doing housework, knitting, caring for her dogs and using cosmetics, perfume, sachet powder and manicuring aids. As a cleanser for her hands liquid petrolatum was prescribed, and a zinc paste containing 5 per cent pyrogallol triacetate was applied to the affected areas. She was instructed to apply this daily and to keep her hands bandaged.

One week later, March 10, 1936, the patient returned. Her hands were markedly worse; the dorsal surfaces, which had heretofore remained unaffected, were now involved, showing a fine vesiculo-erythematous eruption, which was spreading rapidly and caused severe burning and itching. It was evident that the local treatment was making the condition worse. This was discontinued, and the

patient was given a superfatted soap for washing her hands and ordered to protect them at all times with muslin gloves. She was placed on a supposedly nonallergic diet,[5] consisting chiefly of lamb, rice and tea.

On March 20, 1936, the hands were entirely well. Grapefruit was added to her diet. Two days later her hands again became irritated. Grapefruit was ordered discontinued, and the following notation was made on the history: "Look out for sensitivity to citrus fruit. Do not permit patient to handle or eat citrus fruit." Her hands improved quickly, and other foods were gradually added to her diet.

Nothing of importance happened until April 28, 1936, when she cut up tomatoes for a salad. Two days later two small vesicular areas appeared on her hands. Tomatoes were added to the forbidden list.

On June 16, 1936, the patient left for a summer camp in New Hampshire. She returned to Pittsburgh on Sept. 28, 1936. Her hands were then in perfect condition, as they had been during the entire summer. We attributed this to her diet and care in washing, rinsing and drying her hands. She had been kept very busy at camp with domestic duties and was using her hands a great deal.

On Sept. 30, 1936, the patient returned because of an acute recurrence of the vesiculo-erythematous dermatitis affecting all the previously involved areas of the hands, including the dorsal surfaces. There had been no indiscretion in her diet or in the manner in which she looked after her hands. We went over her activities during the preceding two days and found nothing which threw any light on the subject.

The patient mentioned casually that her daughter had just returned from a cruise around the world and had brought some lovely boxes from Japan. Suddenly it dawned on us that perhaps Japanese lacquer had something to do with this acute eruption, but it was difficult to associate with the original eruption.

"Had you any lacquered boxes or lacquered articles before"? was asked. A disheartening no was the answer. Her husband, however, observed that there were some lacquered soup bowls which she had received as a wedding present and which were in use occasionally.

A small place was chipped off one of these bowls and applied as a patch on her lower arm. However, twenty-four hours later, when the patch was removed, there was no reaction. Some of the lacquer was then scraped off, pulverized, moistened and applied as a patch. The next day a highly inflamed, vesicular and extremely itchy area was found where the powdered lacquer had been placed. The reaction was strongly positive.

All the lacquered bowls and boxes were removed from the patient's home, and in a short time the eruption disappeared. It has not recurred, in spite of the fact that all the previously considered irritants have been replaced, the wearing of gloves has been discontinued and dietary restrictions have been removed.

Thus a cruise around the world indirectly led to the discovery of an irritant which otherwise might have remained unsuspected.

631 Jenkins Building.

5. Alvarez, W. C., and Hinshaw, H. C.: Foods That Commonly Disagree with People, J. A. M. A. **104**:2053 (June 8) 1935.

Minor Notes

COINCIDENCE AND DERMATOSES

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On occasion the activities of coincidence must become trying to editors with an abundance of manuscripts that appear to have a largely coincidental background, and dermatologic literature seems to furnish a fertile field for the growth of the coincidence weed. I suppose that where it sticks up its head it is no easy matter to decide how much editorial nourishment, by way of space for publication the weed should receive. Although I realize that too many weeds make an ugly garden, I present still another to plant next to one announcing thrombophlebitis in a patient with pityriasis rosea [1] and another calling attention to lichen planus in a husband and wife.[2]

I trust that some credit will accrue to me for being the first to realize that the contribution I have to make is but a weed in the garden of dermatologic literature and for setting a good example in economy of space to other planters of weeds.

I was consulted in December 1935 by identical twins, white women aged 25, each complaining of an eruption on the right hand and about the outer side of the right ankle. The eruptions started at about the same time in the two patients, were similar in appearance and were almost identical in location. Both patients worked as models for commercial photographers; their likes and dislikes were similar, and both were sensitive to feline emanations. Topical remedies quickly healed the eczema. Unfortunately, opportunity for study of the allergic peculiarities of these twins was not afforded.

1. Reuter, M. J.: Thrombophlebitis and Pityriasis Rosea, Arch. Dermat. & Syph. **35**:1137 (June) 1937.

2. Goodman, J., and Sulzberger, M. B.: Conjugal Lichen Planus, Arch. Dermat. & Syph. **35**:1139 (June) 1937.

DERMATITIS CAUSED BY NUPERCAINE

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The increasing frequency of dermatitis due to nupercaine justifies calling to attention the value of the patch test in patients who have been using an ointment made from the preparation.

In recent weeks I have observed three cases of severe dermatitis following the use of nupercaine ointment, which had been prescribed for the relief of pruritus ani. In each case a patch test was made, the following technic being employed:

An area of the forearm, 5 by 5 mm., is gently scratched, even the presence of serum being avoided. The breaking up of the stratum corneum hastens the absorption of the material to be tested, and the break in the stratum corneum simulates

the condition of parts which have been treated. The ointment is applied to the abraded area and covered with a bit of gauze, which is held in place by wide adhesive. At the end of forty-eight hours the patient reports for inspection of the test site.

Each of the three patients recently tested presented an intensely red edematous area studded with small vesicles. Itching was complained of in from eight to twenty-four hours after the test was made.

Physicians who prescribe nupercaine ointment should test the patient for idiosyncrasy. However, dermatitis from the ointment will continue to be seen, because it is common for laymen to use the ointment for various eruptions.

478 Peachtree Street, N. E.

TREATMENT OF STIES

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PITTSBURGH

Infections occurring about the hair follicles of the eyelids and producing blepharitis or localized abscesses (sties) are at times recalcitrant to treatment. Recurrences are frequent, and attempts to elicit such possible etiologic factors as errors of refraction, metabolic abnormalities and focal infections have been of no avail in most cases.

The following prescription has been used successfully for many years at the McCormick Memorial Hospital in Siam, where blepharitis is prevalent among the natives:

Yellow mercuric oxide.....	2 grains (0.13 Gm.)
Castor oil (tasteless).....	4 minims (0.246 cc.)
White petrolatum	2 drachms (7.39 cc.)

The ointment is applied smoothly over the lids four times a day with an applicator, any débris having been removed carefully prior to the application. It is believed that castor oil, which is used as a lubricant in cosmetics, enhances the chemotherapeutic effect of the yellow mercuric oxide. We have used this formula and have found it of value.

Deficiency of vitamins, especially of vitamin A, was definitely eliminated as an etiologic factor.

From the Pittsburgh Skin and Cancer Foundation.

Clinical Notes

PREVENTION OF DERMATITIS VENENATA DUE TO POISON IVY IN CHILDREN

Further Report

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Last year we[1] reported on the successful use of an alcoholic extract (1:50) of poison ivy made according to the method of Spain and Cooke.[2] The method used in this series was the same as that previously reported. The first dose was 1 cc. of a 1:10,000 dilution of the extract; the second, 1 cc. of a 1:5,000 dilution; the third, 1 cc. of a 1:2,000 dilution, and the fourth, 1 cc. of a 1:1,000 dilution. The remaining doses consisted of 1 cc. of the extract in a 1:500 dilution. In each instance the extract was diluted from the alcoholic extract with sterile distilled water, and the treatments were given hypodermically. Itching at the site of injection was prevented by washing the area with alcohol immediately after the injection.

In the last report the children treated were selected on the basis of results of positive patch tests and of a history of previous attacks. It was recommended that weekly injections be given during the entire season in which poison ivy is prevalent. This year we started the preventive treatments in the middle of the season and treated all the children who had had at least one attack of poison ivy dermatitis during the previous ten weeks. Our experience has been that a child may have several attacks of dermatitis in a season, the number of attacks depending on the frequency of contact. In our environment poison ivy is particularly prevalent, and frequent attacks are common.

Forty-two children were given the injections during the latter part of the last season, and not one child had poison ivy dermatitis during the period of treatment, although in one boy the third attack of dermatitis developed within a few days of his first injection. There were no systemic reactions, and the only local reaction was a mild itching for a few hours at the site of injection. In eight children not treated ivy poisoning developed during this period.

SUMMARY

Forty-two children who were sensitive to poison ivy were given injections of an extract of the plant with excellent results. In one child of this group an acute dermatitis due to poison ivy developed soon after the first injection. In eight children not treated poison ivy dermatitis developed.

The extract of poison ivy used was furnished by Mr. E. Perry, of E. R. Squibb & Sons.

From the New Jersey State Home for Boys and the Medical School, University of Pennsylvania.

1. Molitch, M., and Poliakoff, S.: Prevention of Dermatitis Venenata Due to Poison Ivy in Children, Arch. Dermat. & Syph. **33**:725 (April) 1936.

2. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness: XXVII. Dermatitis Venenata; Observation upon the Use of a Modified Extract from Toxicodendron Radicons (L), J. Immunol. **13**:93 (Feb.) 1927.

News and Comment

INCREASED REQUIREMENTS FOR A CERTIFICATE IN DERMATOLOGY AND SYPHILOLOGY

A syllabus is being prepared by the American Board of Dermatology and Syphilology, (1) to inform the physician who intends to specialize in that field of the material to be covered in his preparation and the methods by which it can be covered, and (2) to aid the medical schools and the dermatologic departments of medical schools and hospitals by outlining the scope of teaching required for specialization in dermatology and syphilology. The syllabus indicates the minimum requirements only, without restricting a teacher who desires to include additional matter or go into greater detail on a particular subject or subjects.

On completion, this syllabus, with its detailed information, will be made available for general distribution.

At present applicants for certification by the board are classed in two groups, as follows: Group A, consisting of physicians who have limited their practice mainly to dermatology and syphilology for ten or more years, including a period of training satisfactory to the board; group B, consisting of physicians who have practiced dermatology and syphilology for at least five years, including their period of training. Such applicants must have had at least two full years of special training devoted exclusively to dermatology and syphilology, including at least one year in a well organized clinic or as an assistant in the private practice of a well known specialist in this field.

Beginning in 1938, the examination of the American Board of Dermatology and Syphilology will include the following subjects related to the skin: histopathology, mycology, physics as related to physical therapy, and allergy.

For group B candidates to qualify for examination between Jan. 1, 1940, and Jan. 1, 1945, the board will require two years of full time planned training in clinical dermatology and syphilology, including the fundamental subjects mentioned.

Beginning in 1940, the examination will include the following additional subjects in relation to the skin: parasitology, serology and embryology.

Beginning Jan. 1, 1945, additional requirements will become effective. By 1940 it is expected that sufficient facilities will be developed throughout the country to provide three years' training of graduate students, in accordance with the minimum requirements suggested by the Advisory Board for Medical Specialties and outlined in the syllabus.

The minimum requirements for specialization in dermatology and syphilology adopted by that board are:

1. A period of study of not less than three years following the internship is required.
2. This period of training shall include systematic postgraduate instruction in the basic sciences which are necessary to the proper understanding of the diseases involved in this specialty. The following fundamental subjects as related to the skin are deemed necessary by the board: embryology, histology, chemistry, physiology, bacteriology, mycology, parasitology, pathology, immunology, serology, pharmacology and materia medica and physics of physical therapy.
3. Two additional years of study or practice are required.

Prepared by the American Board of Dermatology and Syphilology.

Therefore, candidates for certification by this board who begin their training after Jan. 1, 1940, must plan for a three years' course of systematic training as stated in this syllabus.

In 1945 and thereafter admission to examination by this board will be permissible only to applicants with such training. Groups A and B will be abolished, and all candidates will be required to fulfil the same requirements.

SETS OF DERMATOPATHOLOGIC SLIDES AVAILABLE TO BORROWERS

Through the Registry Committee of the American Dermatological Association the Army Medical Museum is now the custodian of sets of representative histologic sections showing pathologic changes of the skin, which may be borrowed by any dermatologist and by candidates for certification by the American Board of Dermatology and Syphilology. It is understood that acceptance of this service by a candidate is entirely optional and cannot influence the board in any way. To insure access to the sets for the maximum number of candidates others may not borrow the sets during the three months preceding the board examinations. These sets cannot be purchased outright.

The sets include material from the more important dermatoses and are accompanied with mimeographed notes describing each slide, furnishing, therefore, a convenient method of preparing for the pathologic part of the examination for certification.

Sets are loaned under the following conditions:

1. A deposit of $25 must accompany the application, $15 of which will be returned on the return to the museum of the sets in good condition. Checks should be made payable to "Registry Account, Army Medical Museum."

2. Fifty cents will be deducted from the deposit for each slide lost or broken.

3. The sets are sent from the museum by express, collect, and must be returned with carrying charges prepaid.

4. The sets must be returned to the museum within six weeks and in any event at least seven days prior to the next examination by the board. This is necessary on account of the limited number of sets, in order to give the greatest possible number of students the opportunity of studying them. A deduction of 50 cents will be made from the deposit for each day that the sets are retained beyond this time. The syllabus may be kept at a price of $2 at the discretion of the loanee. If it is not returned with the slides it will be assumed that he authorizes the deduction of $2 from his deposit.

5. A candidate for examination must not make known to the board that he has borrowed the set. The board will know of this only when it has been notified by the museum that a set has not been properly returned. Candidates who have not satisfied the conditions under which the sets may be borrowed will not be permitted to take the examination.

6. Application for sets must be made by letter, accompanied with a check covering the deposit, to "The Curator, Army Medical Museum, War Department, Washington, D. C."

The Board will notify the museum of those who have been accepted for examination, so that there will be no delay in receipt of sets by the candidates during the restricted preexamination period.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

REINOCULATION WITH THE SPIROCHETES OF YAWS. T. B. TURNER, Am. J. Hyg. **23**:431, 1936.

In man, yaws confers immunity to reinfection. Resistance to auto-inoculation becomes manifest early in the course of the disease and obtains in most persons during the period in which active lesions are present. Immunity to reinoculation with heterologous strains of the spirochetes of yaws develops slowly during the course of the natural disease. Within the first three years reinoculation may give rise to a modified or an abortive attack of yaws, but after a period of ten years the majority of yaws-infected persons are refractory to reinoculation. An interruption of the normal course of the disease by treatment seems to retard the development of immunity. Syphilis also confers immunity to yaws, and this immunity is as great as, if not greater than, that conferred by yaws itself.

FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

A CASE OF CAROTENEMIA AND DIABETES MELLITUS WITH NECROPSY REPORT AND ANALYSES OF LIVER FOR CAROTENE, VITAMIN A, TOTAL FAT AND CHOLESTEROL. A. C. PARIENTE, C. H. PRESENT and E. P. RALLI, Am. J. M. Sc. **192**:365 (Sept.) 1936.

The subject forming the basis of this report was a 45 year old man who had had diabetes mellitus for two years.

The reports of other observations on the incidence of carotenemia and diabetes mellitus are reviewed. The suggestion is made that the excess of carotene following its metabolism would be found in deposits of fat, since carotene is handled in much the same manner as fats.

In the patient the carotene in the blood was higher than normal before carotene was administered. Clinical evidence of the carotenemia was visible when the level of carotene in the blood rose to 0.540 mg. per hundred cubic centimeters.

Deposits of carotene in the mesenteric fat and in the arterial plaques were observed on autopsy.

STUDIES ON TWO CASES OF URTICARIA FROM COLD SENSITIVITY AND OF THE EFFECT OF HISTAMIN TREATMENT. L. L. SAYLOR and I. S. WRIGHT, Am. J. M. Sc. **192**:388 (Sept.) 1936.

In the first of the two cases reported here, it was observed that histamine was liberated at a much higher temperature of the skin than had previously been reported. The patient, a woman, was found to have a skin temperature of 80.2 F. when the reaction occurred. No evidence of allergy was found, although the symptoms were relieved by histamine.

In the second case symptoms developed while the patient, a girl, was swimming in cold water. Unconsciousness followed, and the girl was nearly drowned.

Saylor and Wright think that there are many unrecognized cases of this condition and that the dangers cannot be overemphasized.

JAMIESON, Detroit.

THE PATHOLOGY OF THE AORTA IN HAITIAN TREPONEMATOSIS. C. S. WELLER, Am. J. Syph., Gonor. & Ven. Dis. **20**:467 (Sept.) 1936.

One hundred and sixty-nine aortas obtained from a group of Haitians, many of whom had scars of yaws and a history of the disease and many of whom had a genital scar and a history of syphilis, showed in 65.7 per cent of the aortas histologic lesions which when they occur in inhabitants of the temperate zone are attributed

to syphilis. Spirochetes were demonstrated in microscopic sections of 29.9 per cent of the specimens. The granulomatous changes present were those of syphilitic aortitis.

This study does not offer proof of either the unity or the duality of yaws and syphilis. However, one of three conditions must exist: (1) Yaws and syphilis are essentially the same disease; (2) in the group of patients here considered the incidence of syphilis was so high that the evidence of this disease was overwhelmingly obtrusive; (3) yaws and syphilis, if they are different diseases, produce identical aortic lesions. The third supposition adds another item to the list of attributes which make these two conditions indistinguishable.

MAPHARSEN IN THE TREATMENT OF EARLY SYPHILIS. G. V. KULCHAR and C. W. BARNETT, Am. J. Syph., Gonor. & Ven. Dis. **20**:482 (Sept.) 1936.

This report deals with the clinical study of the arsenoxide mapharsen, in the treatment of early syphilis. However, as mentioned by the authors, the fact that bismuth was used in addition impairs the reliability of their results.

A total of 1,270 injections of mapharsen were given to fifty-six patients with primary or secondary syphilis. Thirty-three of these patients received more than twenty injections of the drug in addition to treatment with a heavy metal.

The healing of the lesions was slightly more rapid than with neoarsphenamine, and reversal of the serologic reactions was somewhat slower than with the arsphenamines. The incidence of involvement of the central nervous system was at least equal to that observed with other arsenicals. Reactions to treatment, particularly those of the gastro-intestinal type, were more frequent than with neoarsphenamine.

REUTER, Milwaukee.

PURPURA HAEMORRHAGICA FOLLOWING THE ADMINISTRATION OF NEOARSPHENAMINE: THE REACTION TO NEOARSPHENAMINE COMPARED WITH THE REACTION TO MAPHARSEN. E. H. FALCONER, N. N. EPSTEIN and G. K. WEVER, Arch. Int. Med. **58**:495 (Sept.) 1936.

Three cases of purpura haemorrhagica following the administration of arsphenamine were studied during the period from 1931 to 1935. Severe toxic constitutional reactions accompanied the changes in the blood in all the cases, and initial sensitivity to the drug existed in two.

The authors believe that the amount of arsenic in the circulation is not the important factor in determining the toxic reaction but that there is probably some product of oxidation formed in the breaking down of the neoarsphenamine.

No untoward symptoms of any kind followed the administration of mapharsen.

They suggest a distant relationship between postarsphenamine nitritoid crises and thrombocytopenic purpura haemorrhagica and stress the importance of blood counts in all patients showing nitritoid crises.

Capillary lesions are as important as thrombopenia in the production of the purpuric manifestations.

JAMIESON, Detroit.

A SYPHILITIC ULCER OF THE EYELID. S. H. MCKEE, Canad. M. A. J. **35**:307 (Sept.) 1936.

McKee reports the case of a man aged 40 who presented an ulcerated area involving the outer two thirds of the edge of the right lower eyelid. Destruction of tissue included that of the tarsal plate. Healing was complete in two weeks as a result of antisyphilitic treatment.

THE RADIOLOGICAL TREATMENT OF CANCER, 1929-1935: IV. CARCINOMA OF THE LIPS. G. E. RICHARDS, Canad. M. A. J. **35**:490 (Nov.) 1936.

In a critical analysis of the after-results of treatment of 335 patients with carcinoma of the lips, Richards found that 84.4 per cent of 300 of these patients

were alive and well and known to be free from recurrence of the disease. Richards considers that radiologic methods are a satisfactory form of therapy in dealing with cancer of the lip and stresses the advisability of early diagnosis and prompt treatment.

THE RADIOLOGICAL TREATMENT OF CANCER, 1929-1935: V. CARCINOMA OF THE TONGUE. G. E. RICHARDS, Canad. M. A. J. **35**:593 (Dec.) 1936.

Richards reports the results of treatment in 101 cases of cancer of the tongue. In 73 per cent, the lesions were advanced. Healing of the primary lesion by radiologic treatment was obtained in 54 per cent of the cases. Control of the disease was obtained in 34 per cent. Richards points out that conservation of tissue is an important consideration in the treatment of lesions of the tongue and that radiologic methods are advantageous in this respect. He feels that there is an urgent need for earlier diagnosis and treatment.

THE RADIOLOGICAL TREATMENT OF CANCER, 1929-1935: VI. INTRA-ORAL LESIONS (EXCEPT THE TONGUE). G. E. RICHARDS, Canad. M. A. J. **35**:599 (Dec.) 1936.

Of 158 cases of carcinoma of the mouth studied by Richards, the point of origin was the alveolus in 60, the floor of the mouth in 30, the buccal mucosa in 55 and the roof of the mouth in 13. While treatment was individualized, radiologic methods were employed principally in the treatment of the primary lesions. When metastases to regional lymph nodes occurred, surgical methods were resorted to, together with roentgen or radium treatment. In 72 per cent of the cases the disease was in the advanced stage when the patient was first seen. The result of treatment showed that 69, or 43 per cent, of the patients were alive and free from symptoms; 5 were alive but not free from the disease; 70, or 44.3 per cent, died of the disease; 10 died of extraneous diseases, and 4 were untraced. Richards stresses the advantage of early diagnosis, since of 29 patients treated during the early stage of the disease, 27, or 93.1 per cent, were cured.

HEMORRHAGIC ENCEPHALITIS FROM NEOARSPHENAMINE IN PREGNANCY: REPORT OF A CASE WITH UNUSUAL WIDESPREAD VASCULAR PARALYSIS. F. E. CORMIA, Canad. M. A. J. **35**:610 (Dec.) 1936.

Cormia reports the case of a pregnant woman aged 23, in whom after three injections of neoarsphenamine had been given there developed fever, general bodily pains and delirium. She became cyanotic, restless and disoriented and lost consciousness. A convulsion developed, and she became spastic and sank into a deep coma. Death occurred after several other convulsions and in spite of various types of treatment. Autopsy revealed syphilitic aortitis, diffuse petechial hemorrhages in the brain with terminal thrombosis and infarction of the medial part of both temporal lobes, exudative cholangeitis, septic splenitis, passive hyperemia of the lungs, productive pleurisy (affecting both lungs), diffuse petechial hemorrhages in serous cavities and parenchyma of the organs of the fetus. Cormia points out that the incidence of hemorrhagic encephalitis is apparently higher in pregnant than in nonpregnant women. He states that the maximum dose of neoarsphenamine to be given in pregnancy should be 0.3 Gm. weekly. He also advises that a patient who has headache, abdominal pain, severe restlessness or nausea about two days after any of the first few injections of an arsphenamine should be watched closely to prevent the onset of hemorrhagic encephalitis.

PRIORITY AMONG AMERICAN PHYSICIANS IN DEMONSTRATING THE CAUSE OF GRAIN ITCH: TARDY CREDIT THEREFOR GIVEN TO DR. LYMAN TALMAGE RAWLES. HERMAN E. KITTREDGE, J. A. M. A. **107**:2109 (Dec. 26) 1936.

According to Kittredge, the first American demonstration that a mite was the cause of grain itch was made by Dr. Lyman Talmage Rawles on May 14, 1909, and he should be considered the original and independent American discoverer of

the cause of grain itch. A month after the work of Rawles was published, Schamberg and Goldberger demonstrated that Pediculoides ventricosus is the cause of grain itch, and they are usually credited with priority for their investigative work. The work of Rawles is considered by Kittredge to be particularly noteworthy because of his lack of investigative facilities; it was probably overlooked because he depended on a laboratory report which apparently misidentified the mite. On the basis of the evidence which he was able to find, Kittredge concludes that in Rawles' paper Pediculoides ventricosus should have been named as the mite causing the disease instead of Ditropinotus aureoviridis, the presence of which was reported.

THE PHARMACOPEIA AND THE PHYSICIAN: THE USE OF ANTISYPHILITIC REMEDIES. H. N. COLE, J. A. M. A. **107**:2123 (Dec. 26) 1936.

Cole states that prophylaxis is the best treatment for all forms of syphilis. He advocates the routine use of the Wassermann test or of a similar flocculation test and repeated tests throughout pregnancy. Adequate and continuous therapy must be administered to patients with early syphilis. In late syphilis, the type of medication and the dosage vary with the age of the infection and with the organs involved in the syphilitic process.

PLANTAR WARTS, FLAPS AND GRAFTS. VILRAY P. BLAIR, JAMES BARRETT BROWN and L. R. BYARS, J. A. M. A. **108**:24 (Jan. 2) 1937.

When plantar warts are resistant to moderate doses of radium or roentgen rays, Blair, Brown and Byars advise their destruction by the actual cautery. The painful sequelae of overexposure to roentgen rays or radium may require only excision of the damaged tissues, or a pedicle flap of full thickness may be necessary to fill in the defect. Orthopedic care of the foot is requisite after the wart has been cured in order to prevent the development of painful calluses. If these develop in spite of this precaution, it is best to excise them and to substitute a plantar flap.

ULCERATIVE LESIONS OF THE SKIN IN LYMPHOGRANULOMA INGUINALE. MAX S. WIEN and MINNIE O. PERLSTEIN, J. A. M. A. **108**:27 (Jan. 2) 1937.

The possibility that ulceration of the skin may occur in lymphogranuloma venereum (inguinale) has not received much consideration in the literature. In a series of 500 cases of this disease Wien and Perlstein noted 12 cases of ulceration of the skin, which they think is a part of the pathologic process. They were able to distinguish three types of ulceration, namely: (1) ulceration of the skin only; (2) ulceration of the skin secondary to an existing involvement of a lymph node; (3) ulceration developing on an esthiomene. The authors differentiated the ulcers from chancroids, granuloma inguinale, syphilis, tuberculosis, gonorrhea, ulcus vulvae acutum, ulcus vulvae simplex chronicum, traumatic ulcer and epithelioma. Cultural examinations showed a nondescript bacteriologic flora, and the histologic study revealed nonspecific ulceration, fibrosis and plasma cell infiltration. Wien and Perlstein feel that when ulcers of the skin of unknown origin occur, especially when they are in the genitocrural area, Frei antigen should be used both diagnostically and therapeutically, in order to rule out the possible relation of the ulceration to lymphogranuloma venereum.

PIGMENTATION OF THE SKIN DUE TO IRON (COPPERAS) APPLIED LOCALLY. RICHARD L. SUTTON JR., J. A. M. A. **108**:112 (Jan. 9) 1937.

Sutton reports the case of a woman aged 33 who used a strong solution of copperas (ferrous sulfate) for the treatment of an impetigo on her neck. Subsequent medical treatment cured the impetigo, but a macular, reddish brown pigmentation of the skin at the sites of the impetigo remained. The pigmentation, which was permanent, was determined by Sutton to be due to the dyeing of the corium with basic ferric acetate.

SYPHILIS OF THE MYOCARDIUM AND CORONARY ARTERIES. JACK C. NORRIS, J. A. M. A. **108**:169 (Jan. 16) 1937.

In a former study, Norris observed evidence of syphilitic heart disease in 20 per cent of 110 patients examined at necropsy and estimated that the myocardium was involved in 20 patients of that group. Since the establishment of an active therapeutic clinic in 1932, there has been a decline of all types of heart disease due to syphilis. Norris states that from 10 to 20 per cent of patients with syphilis of the aorta have involvement of the heart muscle. A more complete investigation may show that every patient with aortic syphilis also has myocardial syphilis. In substantiation of his contention of the specific nature of syphilitic myocarditis were the absence of other organisms and the lack of evidence of hypertensive arteriosclerotic and rheumatic heart disease. In 3 cases which Norris reports, syphilitic cavitations as well as other gross and microscopic changes together with the presence of spirochetes in the heart muscle favored the diagnosis of syphilis of the myocardium.

STREPTOCOCCIC DERMATOSES OF THE EARS. JAMES H. MITCHELL, J. A. M. A. **108**:361 (Jan. 30) 1937.

According to Mitchell, many of the eczematous eruptions in and around the ears are due to the invasion of streptococci. He agrees with the opinion of Sabouraud, who named such manifestations *streptococcides eczématiformes*. Besides causing a retro-auricular intertrigo, the streptococci may cause the formation of scaly, exudative patches in the cavum and in the canal. Itching is a common complaint. The diagnosis must be verified by laboratory tests. Demonstration of streptococci in serum from fissures and in the squama-like crusts is readily made. Cultures are more difficult to make, and Mitchell advocates the use of brain broth-dextrose medium in tubes at least 12 inches (30.4 cm.) long. In the cases described by Mitchell no fungi were observed, and the possibility of external irritants was excluded.

CANCER OF THE LIP: RESULTS OF THERAPY IN FOUR HUNDRED AND TWENTY-FIVE CASES FOLLOWED FROM ONE TO TEN YEARS. U. J. WILE and E. A. HAND, J. A. M. A. **108**:374 (Jan. 30) 1937.

In a study of the results of therapy in 425 cases of carcinoma of the lip, Wile and Hand found that in the cases of early involvement local destruction or surgical removal and dissection of the regional lymph nodes gave the best results. The results of surgical excision alone or of radium therapy were good, but roentgen therapy alone gave indifferent results. In the treatment of moderately advanced lesions the best results were achieved by surgical excision together with dissection of the suprahyoid nodes. Prior treatment, including inadequate roentgen therapy, lessened the chances for recovery. Metastases were rarely found without palpable lymph nodes, and for this reason the authors believe that surgical intervention is not indicated unless the nodes can be felt. High voltage roentgen therapy to the regional lymph nodes was held to be unnecessary in cases in which there were no palpable nodes and in those in which no metastasis had occurred.

LEWIS, New York.

DIAGNOSTIC MEASURES IN ATOPIC INFANTILE ECZEMA. HERBERT J. RINKEL, South. M. J. **29**:507 (May) 1936.

The diagnosis of the precipitating causes of atopic eczema is essentially that of food allergy. The possibility of allergy in any case of eczema cannot be eliminated until all the diagnostic measures have collectively indicated that there is no relation between the symptoms and the diet.

The accuracy of cutaneous testing is approximately 50 per cent in cases in which there are cutaneous reactions, while in 20 per cent of those in which

eczema is present no reaction is obtained. The scratch method is superior to the intracutaneous method on a basis of specificity.

Elimination diets must be used with due regard to the botanical relationship of foods, since two of every five sensitizations are complete for the botanical food group.

Diet and symptom records in the author's hands have revealed twice as many causes of eczema as were revealed by cutaneous testing and represent a most valuable diagnostic measure. Clinical observation is a necessary procedure in every case as a check for all laboratory tests employed.

The leukopenic index is of distinct aid, since it may be used regardless of the clinical state of the eczema. Its accuracy has been found to be the same for eczema as for other types of food allergy; it is approximately 84 per cent.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

LYMPHOGRANULOMA INGUINALE. C. L. WILMOTH, J. Trop. Med. **39**:173 (Aug. 1) 1936.

Wilmoth reports briefly some attempts made in 1930 and 1931 to transmit lymphogranuloma venereum to rabbits.

Reasoning from the results of other experiments, he suggests that the disease cannot be readily transmitted between human beings except during the short duration of the primary lesion. He considers the virus from the lymph nodes to be noninfective or at least rarely infective.

No method of treatment is suggested offering any advantage over those already known.

He advises early diagnosis by means of the Frei test and early excision of the affected glands.

DISEASES OF THE SKIN IN NEGROES. L. J. A. LOEWENTHAL, J. Trop. Med. **39**:209 (Sept. 15) 1936.

In the first instalment of this article Loewenthal comments on the structure of the Negro skin, the sweat and sebaceous glands, the hair and the nails with reference to distinctions between the white and the Negro skin.

The physiology is considered in part 2—especially the regulation of temperature and the effects of light.

The article will be continued. JAMIESON, Detroit.

VARIATIONS IN THE PATHOGENICITY OF THE SPIROCHETE OF SYPHILIS. C. LEVADITI, A. VAISMAN, R. SCHOEN and Y. MANIN, Ann. Inst. Pasteur **56**:251, 1936.

A study of the Truffi strain of spirochetes, the activity of which was traced from 1908, indicated marked attenuation so far as pathogenicity for man or anthropoids is concerned. Two laboratory accidents and one inoculation in a human volunteer permitted some conclusions to be drawn regarding the pathogenicity of this strain for man. Local lesions were produced, but there was little apparent tendency to spread. Observations of mice inoculated subcutaneously indicated that infection of lymph nodes is not dependent on presence of the virus in the blood stream. Such inapparent infection of mice was not successfully transmitted in series. The development in situ of a "vegetative" form of the virus was said to account for the presence of the spirochetes in the peripheral lymphatic system. The report is extended to present further studies of the two phases of the syphilitic virus, the invisible aspirochetal and the vegetative spirochetal phase. The latter is believed to develop in the same manner as the former, regardless of the form present in the inoculum. These phases were studied microscopically, and an intermediate stage characterized by twisted loops was noted. The resistance to gamma rays, rays from the mercury vapor arc and glycerin appeared equal.

MARSHALL, Berkeley, Calif. [ARCH. PATH.]

SCLEREDEMA OF ADULTS. A. TOURAINE, R. RABUT, L. GOLÉ and SOULIGNAC, Bull. Soc. franç. de dermat. et syph. **43**:1634 (Nov.) 1936.

The authors state that in France scleredema adultorum is not well known among dermatologists. A typical example of the disease in a woman aged 46 is reported. The induration of the skin appeared on the neck and upper portions of the trunk about two weeks after an attack of acute angina accompanied by malaise and pains in the joints. Involution resulted within six weeks after the onset. The hands and feet were not involved.

ANGIOMATOUS NEUROFIBROMA OF THE BACK. THIBAUT and FRABOULET, Bull. Soc. franç. de dermat. et syph. **43**:1763 (Dec.) 1936.

The authors described an unusual hard tumor, measuring 12 by 15 cm., which occurred on the back of a man aged 53. There were no signs of metastases or cachexia two and a half years after the onset of the lesion; this pointed against a diagnosis of ordinary sarcoma. Mycosis fungoides d'emblée and dermatofibrosarcoma (Darier) were ruled out histologically.

The histologic section showed that the growth should be classed with the neurofibromas. Sections showed numerous blood vessels situated in a mass of elongated, fusiform cells and connective tissue fibers. There were no evidences of malignant degeneration.

SCLERODERMA WITH CALCAREOUS DEPOSITS AND ULCERATION (SYNDROME OF THIBIERGE AND WEISSENBACH). A. SÉZARY, R. WEISSENBACH, R. ISRAËL and W. STEWART, Bull. Soc. franç. de dermat. et syph. **43**:1776 (Dec.) 1936.

The authors discuss a case of scleroderma which was unusual on account of the abundance of calcareous deposits and the presence of ulcers on the legs. The patient was a woman aged 58 who came to the hospital for treatment of the ulcers. The scleroderma had begun when the patient was 30 and was of the diffuse type, involving the hands, the feet, the upper and the lower extremities and the trunk. Numerous calcareous deposits were present on the thighs and forearms. Many more such deposits could be visualized by roentgenograms than were apparent clinically.

EOSIN IN THE LOCAL TREATMENT OF PSORIASIS. GOUGEROT and DEGOS, Bull. Soc. franç. de dermat. et syph. **43**:1784 (Dec.) 1936.

The authors used alcoholic and aqueous solutions and other preparations of various dyes, such as crystal violet, fuchsin, methylthionine chloride (methylene blue) and eosin in the treatment of psoriasis. The most favorable results were obtained with eosin in the following concentrations: 2, 5 and 10 per cent solutions in water, 1 and 2 per cent solutions in alcohol, 2 per cent mixture in petrolatum and 2 per cent mixture in cold cream.

The lesions were either painted in a 2 per cent solution of eosin in alcohol every two days and anointed with petrolatum or with a cold cream on the alternate days or treated daily with 2 per cent eosin in petrolatum or in a cold cream. During the treatment the patients were instructed to bathe two or three times a week, using 125 Gm. of sodium carbonate per bath, between applications of eosin. The results were encouraging: The scales disappeared rapidly, and the lesions faded within two weeks. The authors felt that eosin gave results more favorable than those obtained with juniper tar or with salicylic acid and equal to those obtained with chrysarobin. Eosin has no odor and is easily washed off. The local therapy was combined with a fat-free diet; the eosin was applied vigorously for several minutes. In the opinion of Gougerot and Degos this method minimized recurrences better than any other treatment.

LAYMON, Minneapolis.

THE TREATMENT OF LEPROSY WITH METHYLTHIONINE CHLORIDE (METHYLENE BLUE). G. BERTACCINI, Gior. ital. di dermat. e sif. **77**:561 (Aug.) 1936.

Twenty-five patients with leprosy were treated by means of intravenous injections of methylthionine chloride. None of them showed any striking improvement, and the author concluded that the therapeutic value of that drug in the treatment of leprosy is inferior to that of most of the other agents employed in this disease. In spite of the fixation of the dye on the bacilli, the latter show little or no changes in their vitality.

PUSTULAR PSORIASIS. M. COMEL, Gior. ital. di dermat. e sif. **77**:577 (Aug.) 1936.

Comel reports a case of inveterate psoriasis with pustular lesions on the lower extremities. The pustules were situated on the plaques of psoriasis and histologically the involvement was in the stratum Malpighii. Comel believes that pustular psoriasis is a clinical form of the disease in which exudation is the most important feature and that it is probably due to internal factors still undetermined.

SOLITARY XANTHELASMOID FIBROSARCOMA OF THE SKIN: REMARKS ON THE SO-CALLED HISTIOCYTOMA OF THE SKIN. E. SCOLARI, Gior. ital. di dermat. e sif. **77**:589 (Aug.) 1936.

The patient was a baby aged 3 months in apparently perfect health. On the supraclavicular region a tumor the size of a walnut developed in the course of a few weeks. Histologic examination showed the lesion to be composed of connective tissue cells loaded with lipids, mostly true fats, and justified the diagnosis of fibrosarcoma. The protoplasm of many cells was filled with droplets of fat which gave them the appearance of xanthoma cells. In some respects the histologic picture corresponded to that of the condition described as histiocytoma cutis. The presence of lipids in the connective tissue cells in this case suggests the hypothesis that they may be the product of altered cellular metabolism and not the result of phagocytic activity.

PRIMARY CUTANEOUS TUBERCULOSIS IN ADULTS: REPORT OF A CASE OF PRIMARY TUBERCULOUS ULCERATION OF THE SKIN. P. PINETTI, Gior. ital. di dermat. e sif. **77**:597 (Aug.) 1936.

Pinetti reports the case of a man aged 23 who presented a primary tuberculous ulceration of the skin. No visceral tuberculosis could be demonstrated either clinically or roentgenologically. The lesions consisted of an ulcer the size of a penny situated on the bridge of the nose and of suppurating adenitis of the left side of the jaw. Histologically a typical tuberculous structure was demonstrated, but no tubercle bacilli were isolated from the ulcer. From the lymphatic glands numerous bacilli were obtained, and inoculations of guinea-pigs gave positive results. Although this case seemed to be one of primary tuberculous infection of the skin, Pinetti points out the difficulties of ruling out systemic tuberculosis and concludes that in any case the question of the original site of the infection remains doubtful.

MULTIPLE STEATOCYSTS OF THE PILOSEBACEOUS FOLLICLES (BOSSELLINI), SEBOCYSTOMATOSIS (GÜNTHER). B. FRACCARI, Gior. ital. di dermat. e sif. **77**:977 (Dec.) 1936.

The condition under consideration, characterized by the presence of numerous sebaceous cysts in the follicular pilosebaceous system, was described by Bossellini in 1898, who arrived at the following conclusions: The formation of these cysts is due to a process of cornification which prevents the normal secretion of the sebum; the sebaceous matter collects at the point of junction of the duct with the hair follicle, causing a dilatation which eventually becomes a cyst; this dilatation is always situated in the follicle, and the gland itself takes no part in its formation; the cyst remains quiescent as soon as the formation of sebum ceases, owing to

atrophy of the gland; the gland atrophies as a result of pressure between the cyst and the adjacent connective tissue. The case of multiple sebaceous cysts on the scalp and face studied by Fraccari led him to believe that there is a mechanism, probably of endocrine nature, by which the secretion of sebaceous matter is altered. Histologically he describes two types of cysts, one follicular and one glandular. In the latter, the walls of the cysts were seen to consist of active acinous glands with secretory power. Fraccari believes that in cases of this condition there is a tumultuous production of sebum which accumulates in the gland itself, as well as in the follicle, causing the two types of cysts reported.

PARDO-CASTELLO, Havana, Cuba.

HYPOTHYROIDISM OF SYPHILITIC ORIGIN. MANUEL BLANCO OTERO, Arch. españ. de pediat. **20**:87 (Feb.) 1936.

Blanco Otero reports the occurrence of this comparatively rare pathologic anomaly in a child 4 years old. The hereditary syphilitic manifestations consisted mainly of periostitis, manifested particularly in the upper extremities. The cretinic manifestations were marked, particularly the facial and somatic characteristics and retarded development of the carpal bones. The stature of the child corresponded to that of a child of 19 months, but the mass development corresponded to that of a child of 4 years. The author is of the opinion that the syphilitic infection was the responsible etiologic factor in the development of the endocrine dysfunction.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

HIPPOCRATIC FINGERS AND THE BAMBERGER-MARIE SYNDROME. NORBERTO QUIRNO, Rev. méd. latino-am. **22**:257 (Dec.) 1936.

Quirno has investigated the diagnostic value of capillaroscopy in cases of hypertrophic osteo-arthropathy, or the Bamberger-Marie syndrome. This deformity of the fingers has been attributed to capillary dilatation and resulting congestion in cases of chronic pulmonary or cardiac disease. Quirno made capillaroscopic studies on twenty-four patients, of whom seven had cancer of the lung, two congenital heart disease, one syphilis of the lung, two bronchiectasis, one a chronic pulmonary abscess, one pyopneumothorax, four chronic tuberculosis and the rest other thoracic and abdominal conditions. In all the patients alterations in the distribution, number or size of the capillaries were demonstrated. However, no distinctive changes were recorded which could be attributed to the syndrome under investigation. Quirno concludes that the alterations of the capillaries are not the sole cause of the hippocratic deformities. Other factors are being investigated.

PARDO-CASTELLO, Havana, Cuba.

TRAUMATIC OCULAR HERPES ZOSTER. E. AMMANN, Klin. Monatsbl. f. Augenh. **95**:793 (Dec.) 1935.

Ammann discusses the literature on traumatic herpes zoster of the cornea. He refers to the controversy between Grüter and Schönfeld. Grüter succeeded in producing an eruption of typical herpes zoster by injecting brain substance from animals which were infected with herpes. Schönfeld and other writers, while denying the identity of the original viruses in these experiments of inoculation, admit that these viruses are related. To illustrate the relation between several types of herpes Ammann refers to an observation of his own. A girl of 8 years with typical scars of dendriform keratitis presented herpes simplex of recent occurrence. Eleven years later she presented herpes zoster on both eyelids, on the corneas and on the forehead, i. e., in the area of the first and second branches of the trigeminal nerve of the same side. Was the age, Ammann asks, instrumental in causing the virus to act dermatropically at first and neurotropically later?

Sufficient proof has been furnished recently, in Ammann's opinion, for the close relation between herpes zoster and forms of varicella. The virus of herpes simplex

is identical, in his mind, with that of herpes zoster. It is known that herpes zoster may develop as a consequence of direct or indirect damage of large nerves, of the spinal cord or of the spinal ganglions and posterior roots. He quotes briefly the published reports of seven cases and reports an eighth case in support of his view that even a slight lesion of the head may be followed by herpes zoster. Some questions will have to be settled: Is the virus a living or an enzymic substance? Is its origin exogenous and does it wander from the wound along the nerves to the gasserian ganglion, or is it endogenous and attracted by the nerves and ganglions through increased neurotic irritation?

The observations prompt Ammann to adopt the opinion that both ophthalmic herpes zoster and simple corneal herpes may be caused by injuries.

STOLL, Cincinnati. [ARCH. OPHTH.]

NEW FORMATION OF LYMPHOID TISSUE IN MYCOSIS FUNGOIDES, K. H. ZINCK, Virchows Arch. f. path. Anat. **296**:319, 1935.

Necropsy of a 63 year old man with the external lesions of mycosis fungoides revealed granulomatous nodules of characteristic histologic appearance in the lungs, heart, stomach, duodenum, right adrenal gland and inguinal lymph nodes. The vegetative nervous system, the peripheral nerves and the organs of internal secretion with the exception of the right adrenal gland were not involved. In the histologic examination especial attention was paid to the reticulum of the granulomas. Most previous investigators have held that the reticulum of the granuloma is formed by splitting of the preexisting connective tissue by the infiltrating cells. Zinck's studies lead him to conclude that the reticulum is newly formed and is an essential part of the granulomatous tissue. He believes that the latter is derived from perivascular indifferent mesenchyme, proliferation of which results in differentiation along various lines. Such a process would account for the formation of reticulum by reticulo-endothelial cells and for the presence of the lymphocytes, plasma cells and other cellular elements of the granuloma.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

ANNULAR HEMORRHAGE IN THE SKIN IN INFANTILE ACRODYNIA (FEER). B. DRAGIŠIĆ, Ztschr. f. Kinderh. **55**:721, 1933.

Dragišić reports the case of a 3 year old boy with infantile acrodynia (Feer) in whom annular bleeding occurred in the skin. According to the author, this manifestation of infantile acrodynia has never before been recorded.

LEVINSON, Chicago. [AM. J. DIS. CHILD.]

SUBCUTANEOUS FAT NECROSIS OF THE NEW-BORN. J. ZIMÁK, Bratisl. lekár. listy **15**:617 (March) 1935.

Zimák reviews the literature, which contains reports of 152 cases, including the present one. In discussing the etiology, he mentions the trauma of difficult labor, angiotrophic reaction, deviation of internal secretions, infection and hypercholesteremia. In the detailed report of a case he cites the first subcutaneous changes on the third day of life following a difficult delivery with high-placed forceps. Various substances, such as solution of aluminum acetate, were applied to the indurated areas. The tendency is toward gradual restitution, but in this instance the baby died of associated bronchopneumonia on the twenty-fourth day of life. The disease may be reproduced in animals by subcutaneous injections of palmitic acid. The conditions considered in the differential diagnosis may include erysipelas, phlegmonous infiltration, subcutaneous abscess and scleroderma.

STULIK, Chicago. [AM. J. DIS. CHILD.]

CHANGES IN THE CEREBRO-SPINAL FLUID IN LATENT SYPHILIS, PARTICULARLY IN RELATION TO TREATMENT. T. UEDA, Jap. J. Dermat. & Urol. **40**:123 (Sept.) 1936.

During a period of three years Ueda investigated the cerebrospinal fluid of 190 patients with latent syphilis. The positive findings in the order of frequency were as follows: a positive gold colloidal reaction in 24 per cent of the cases, an increase in the total protein in 23 per cent, a rise in globulin in 20 per cent, an increase in the number of cells in 16 per cent and a positive Wassermann reaction in 5.3 per cent.

The Wassermann reaction of the blood serum was positive in 138 patients (72 per cent). In the cerebrospinal fluids of these patients whose serum reactions were positive there were more and greater pathologic changes than in the cerebrospinal fluids of those whose serum reactions were negative. Pathologic changes were present in the cerebrospinal fluids of 38 per cent of the patients whose serum reactions were positive and whose syphilis was in the late latent stage and in 26 per cent of those with positive serum reactions whose syphilis was in an early stage. In no case was there only one positive reaction. In no case of early latent syphilis were all five reactions positive; in the cases of late latent syphilis all five reactions were frequently positive. The Wassermann reaction of the cerebrospinal fluid was negative in all cases of syphilis in an early stage while the reaction was positive in 9 per cent of the cases in the late stage. There was no difference in the proportions of the Wassermann and Browning reactions, but the proportion of positive Murata reactions to the former was 30 per cent only. Of patients who started to receive antisyphilitic treatment several years or decades after infection, 38 per cent showed all three reactions positive as contrasted with 15 per cent of those whose treatment was administered early.

NUTRITIONAL ALLERGIC DERMATOSES AND THE CONDITION OF THE DIGESTIVE ORGANS. S. KITAMURA, M. MURAYAMA, K. YAJIMA, K. MORI and T. UCHIMURA, Jap. J. Dermat. & Urol. **40**:167 (Nov.) 1936.

The authors investigated the condition of the digestive organs in patients with allergic dermatoses. Among twenty-five patients they found gastric anacidity in two, and hypo-acidity in seventeen. Of fourteen patients examined with the intravenous galactose method, eleven showed a disturbance of the hepatic function. Of twenty patients with hemoclastic crisis, thirteen showed a positive reaction to the tests. In five cases in which the feces were examined the authors found poor digestion and marked putridity or fermentation. The authors are of the opinion that anacidity or hypo-acidity of the gastric juice and disturbance in the function of the liver are important factors in the pathogenesis of nutritional allergic dermatoses.

INFLUENCE OF ECZEMATOUS CHANGES IN THE SKIN ON THE KIDNEY: FAT DEPOSITION IN THE KIDNEY OF THE RABBIT IN EXPERIMENTAL DERMATITIS. NAOMI TANAE, Jap. J. Dermat. & Urol. **40**:170 (Nov.) 1936.

The author observed that in rabbits with experimental dermatitis there occurred during the acute stage changes in the kidney consisting of diffuse stasis in the parenchyma, swelling of the protoplasm, poor staining of the nuclei and deposition of fat in the epithelial cells of the tubules. The intensity of these changes diminished in proportion to the decrease in the dermatitis and finally disappeared entirely.

TRANSMISSION OF LYMPHOGRANULOMA VENEREUM TO MICE AND GUINEA-PIGS BY INTRACEREBRAL INOCULATION. YUSO SATO, Jap. J. Dermat. & Urol. **40**:187 (Nov.) 1936.

The author succeeded in transmitting the virus of lymphogranuloma venereum by intracerebral inoculation to monkeys, white mice and guinea-pigs. The inocula-

tion material consisted of an emulsion of glands of two patients with lymphogranuloma and of the brain of a monkey (Macacus brevicaudus) which was infected with virus of lymphogranuloma venereum. The material was diluted ten times with physiologic solution of sodium chloride and sterilized, and 0.02 cc. was inoculated intracerebrally.

Half of the mice presented, mostly from three to five days after inoculation, symptoms of anorexia, laziness, irritability, poor growth of hair, paresis of the posterior extremities and disturbance in balance. Death followed in a few days. Histologically meningo-encephalitis was noted in the clinically affected as well as in the symptomless animals. The antigen prepared from the brain of these animals gave a positive Frei reaction in patients with lymphogranuloma venereum while preparations of the brain of normal mice gave a negative reaction. The author succeeded in transferring the virus in ten passages by intracerebral inoculation of an emulsion of the brain of the infected mice. With each passage the virus became weaker, and it finally ceased to show any virulence.

Most guinea-pigs showed clinical symptoms from three to four days after inoculation. In contrast to the infected mice, the guinea-pigs did not run away when suddenly slapped by the experimenter. Histologically, meningo-encephalitis was observed, and an effective Frei antigen could be prepared from the brain of the infected animals. The author succeeded in transferring the virus to guinea-pigs in four passages. He found, however, that the mortality of guinea-pigs was rather large owing to the trauma of inoculation.

BLOOM, New York.

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

JOHN E. RAUSCHKOLB, M.D., *President*

Sept. 24, and Oct. 29, 1936

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Congenital Syphilis with Multiple Gummas and Healed Iridocyclitis.
Presented by DR. G. W. BINKLEY.

T. C., a man aged 27, from the service of Drs. Cole and Driver at the City Hospital, was told that he had inherited syphilis from his mother, and that he had been given some treatment at the age of 5 years. No subsequent treatment for the disease has ever been given. Fourteen months ago there developed on the right arm a running sore, which healed after local application of mild mercurous chloride. Since then similar lesions have developed, and these show a tendency to slow, spontaneous healing.

Distributed irregularly over the extremities and the neck are several coin-sized soft, rubbery cutaneous and subcutaneous nodules. There are some soft, smooth scars of previously healed lesions. On the nape of the neck there is a nodular necrotic destructive lesion showing a tendency to central healing. A biopsy specimen was taken from a nodule on the right arm.

Examination of the eyes revealed a healed bilateral iridocyclitis with posterior synechiae. Neurologic examination revealed nothing abnormal. Examination of the heart revealed no abnormal findings. The Wassermann and Kline tests of the blood were strongly positive. Examination of the spinal fluid gave negative results.

Histologic examination showed mild hyperkeratosis. The epidermis presented a moderate perinuclear liquefaction, while in the upper part of the corium, around the vessels and the sweat glands, were dense nests of mononuclear cells. Giant cells were present throughout the corium.

Stains for Spirochaeta pallida gave negative results.

DISCUSSION

DR. J. R. DRIVER: Assuming that this case is one of congenital syphilis, I find it interesting to see so many gummatous lesions in a person 27 years old. Such a finding would be more likely in a case in which the disease had been more recently acquired.

DR. H. G. MISKJIAN: The possibility of acquired syphilis in a person with congenital syphilis should be considered. Definite primary lesions have occasionally been observed in cases in which there were definite stigmas of congenital syphilis.

DR. H. N. COLE: Such an active process is possible, but nevertheless unusual, at the age of 27 in a patient with prenatal syphilis. Investigations by the Cooperative Clinical Group have shown that patients with prenatal syphilis, even up to the age of 25, may have a picture such as that in this case. On the other hand, if treatment has been carefully given, practically all such difficulty in later life will be eliminated.

Pigmentation After Phenobarbital Eruption. Presented by Dr. G. W. Binkley.

R. S., a man aged 43, from the service of Drs. Cole and Driver at the City Hospital, while a patient in the surgical division of the hospital received on July 24, 25 and 26, 1936, 0.2 Gm. of phenobarbital. On July 27 a generalized scarlatiniform eruption developed. This was accompanied with malaise and fever and gradually subsided over a period of a few days. On August 5 another dose of phenobarbital was given by accident, and this precipitated an acute, and much more severe flare-up of the eruption, associated with dermatitis and edema of the face, the hands and the feet. After the eruption began to subside, at the end of a week or ten days, pigmentation was noted. On August 28 a third dose of phenobarbital was given through error, and an even more acute exacerbation followed, resulting in severe schock. The patient recovered, and he now has a deep generalized pigmentation of the entire body, resembling argyria or Addison's disease. On September 1 the red blood cells numbered 2,500,000 and the white cells 13,600. The hemoglobin content was 50 per cent, and the differential count showed 70 per cent polymorphonuclear leukocytes, 7 per cent small mononuclears, 4 per cent transitional cells, 18 per cent eosinophils and 1 per cent basophils.

Histologic examination showed moderate hyperkeratosis and irregular acanthosis of the epidermis and conspicuous spongiosis in the corium. The blood vessels were dilated and surrounded by a sheath of polymorphonuclears, mononuclears and eosinophils. There was little intracellular and extracellular pigment just beneath the basal layer.

DISCUSSION

Dr. Claude Bazil Norris, Youngstown, O.: This striking pigmentation after administration of a derivative of barbituric acid is unusual and shows the danger of assuming that one can give such drugs indiscriminately. One gets the impression here of severe argyria, the patient being almost as dark as a Negro. It is hard to believe that he was once white.

Dr. J. R. Driver: I had the privilege of seeing this patient during the first reaction from phenobarbital. That reaction was more or less typical of eruptions seen in those having an idiosyncrasy to the drug. The severe second attack following an additional dose of the drug was the most severe reaction of its type that I have ever seen. However, the shocklike reaction and the marked pigmentation following a subsequent dose should serve to remind the members of the disastrous results that may ensue from the subsequent administration of a drug to which a patient may be sensitized.

Dr. R. E. Barney: The pigment that has resulted from this unusual reaction is more like the type seen in Addison's disease than that in argyria. It would be interesting to know what effect such a severe reaction has had on the adrenals.

Dr. C. L. Cummer: Is there any record of examinations of the blood while the patient was in the surgical division?

Dr. G. W. Binkley: The patient's blood count showed approximately 4,000,000 red cells when he was in the surgical division. Anemia has increased considerably since the onset of the dermatitis medicamentosa.

Dr. H. N. Cole: It must be remembered that phenobarbital is a derivative of coal tar. While the condition is somewhat more rare, this reaction may be of the same type as that seen from preparations of phenolphthalein. This man is one of those sensitized subjects in whom the process, instead of being localized, goes on to universal involvement. Further studies are contemplated, in order that the character of pigment present here may be determined. Is it due to iron or to some other cause? I am of the opinion that this condition is an iron pigmentation, resulting from destruction of red blood cells.

Dr. John E. Rauschkolb: If the extensive pigmentation present in this case were an iron pigmentation resulting from destruction of red blood cells, I believe there would be more evidence of icterus, which is not present in this patient.

Phagedenic Ulceration of the Skin. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

M. C., a man aged 38, a file clerk, bruised his right wrist in January 1932. Superficial ulceration resulted, and the axillary nodes became enlarged, suppurated, and were incised and drained. The axillary lesion refused to heal; sinuses developed, and a sluggish ulceration of the skin resulted. In December 1933 implantation of maggots was employed, but only moderate improvement resulted. The ulceration became more extensive, healed in the center and extended at the borders, advancing to the periphery and undermining the border. In the following three and one-half years healing did not occur, and the patient was seen by many physicians and hospitalized in various institutions. Histologic examinations always showed a picture of chronic inflammation. He has lost approximately 20 pounds (9 Kg.).

Over the right shoulder, the right axilla and the right scapular region there is a huge reniform ulceration with a scarred center and extensive borders, showing a granulating and undermined edge, from which a large amount of pus discharges. General physical examination revealed no abnormality. Careful examination and roentgenograms of the lungs, as well as routine examinations of the blood and the urine, showed nothing abnormal. Smears and cultures revealed Staphylococcus albus. Donovan bodies were searched for but not found. Repeated examinations for fungi gave negative results. Examination of the discharge from the lesion and of the stools revealed no amebas. A roentgenogram of the right shoulder and humerus showed some rarefaction of the bone. Serologic tests for syphilis, tuberculin tests with concentrations as low as 1:100 and Frei and chancroidal tests gave negative results. No tubercle bacilli were found on repeated examinations of smears, and inoculations in guinea-pigs revealed no sign of tuberculosis.

Histologic examination showed thinning of the epithelial layer, with irregular prolongation of epithelial masses into the underlying connective tissue. There was degeneration of epithelial extensions but no evidence of a tumor. The bulk of the tissue was composed of poorly organized, diffusely infiltrated granulation tissue, with mononuclear cells predominating. There was diffuse infiltration of polymorphonuclear cells and in some areas of small giant cells. There were a few areas of focal necrosis but no evidence of tubercle formation.

Treatment has consisted of compresses of potassium permanganate, applications of methylrosaniline and ointments of cod liver oil and roentgen and ultraviolet irradiation. The patient was also given several injections of neoarsphenamine and a few treatments with a gold compound. The Gerson diet was instituted, and liver extract and a cod liver oil concentrate were prescribed. None of these measures have affected in any material way the progress of the disease.

DISCUSSION

DR. E. W. NETHERTON, Erie, Pa.: I agree, without much question, that this case is one of chronic phagedenic ulceration. The condition is seen occasionally and is due to staphylococci and streptococci.

DR. H. N. COLE: We have come to the conclusion that the only possible diagnosis is phagedenic ulceration, although we have always kept in mind the possibility of tuberculosis, and the treatment of the patient at the present time is directed along that line.

DR. J. R. DRIVER: After the dressing with cod liver oil a definite but only temporary improvement resulted.

Keratosis Blennorrhagica (Questionable). Presented by DR. H. G. MISKJIAN.

R. S., a man aged 31, had gonorrhea in 1934 and again in 1936. In May 1936 a penile lesion appeared and dark field examination for Spirochaeta pallida gave positive results. The Wassermann test was not made at that time. Over a period of several weeks the patient received seven injections of neoarsphenamine. Treat-

ment lapsed, but shortly afterward a generalized eruption appeared over the body, and antisyphilitic treatment was resumed. Up to September 12, at which time the patient came under my care, he had received a total of twenty-nine injections of neoarsphenamine and six injections of a bismuth compound. The eruption persisted, and at the present time it is limited chiefly to the lower extremities, with a few lesions on the trunk.

The lesions consist of copper-colored flat papules and nodules having an average diameter of 1 cm. The more recent lesions are devoid of scaling, while the older ones are covered with thick, adherent scales. Some of them are moist. In the region of the ankles the eruption is almost confluent, with thick yellowish gray, dirty hyperkeratotic scales and crusts. On the soles are a number of deep-seated papules and nodules. There are some erythematous patches on the glans penis. There are no lesions on the mucous membranes; there is no remarkable adenopathy. Dark field examinations of material secreted from the lesions failed to reveal S. pallida. The Wassermann and microscopic precipitation tests of the blood were negative.

Histologic examination of a medium-sized papule showed a superficial inflammatory process occupying the epidermis and the papillary layer of the corium. There were parakeratosis on the surface and acanthosis deeper down. The interpapillary projections were elongated, and the tops of the papillae were close to the surface. The dense cellular infiltration of the epidermis had dissociated the epithelium to such an extent that changes could be observed only on the periphery of the papule. The papillae showed some edema and congestion, along with some diffuse spongiosis of the malpighian layer. The cellular infiltration was mostly lymphocytic, but a number of polymorphonuclear cells were also present. No plasma cells were found. Around the subpapillary blood vessels was a thick accumulation of lymphocytes, intermingled with histiocytes. The deeper portion of the corium was normal. On the theory that the case might be one of arsenoresistant syphilis, the patient was given ten intravenous injections of mercuric cyanide, 0.01 or 0.02 Gm. each. No influence on the eruption was noted.

DISCUSSION

Dr. John E. Rauschkolb: Many of the lesions present features more or less characteristic of keratosis blennorrhagica. There is prostatic involvement, although there is no evidence of gonorrheal arthritis. Clinically, the eruption is suggestive of keratosis blennorrhagica.

Dr. H. N. Cole: The generalized character of the eruption in some respects suggests allergy to a drug. However, I am inclined to believe that the condition is a resistant cutaneous relapse in syphilis. In addition to intensive antisyphilitic treatment, foreign protein therapy might be of value.

Dr. H. G. Miskjian: I believed this condition to be a resistant cutaneous relapse of the patient's syphilis, but dark field examinations of the lesions gave negative results, and treatment has had no beneficial effect. I have been much puzzled about the condition, and after studying the case for a considerable time, I have been more and more impressed with the clinical evidence in favor of keratosis blennorrhagica.

Note.—The condition was found later to be syphilitic and finally responded to arsenical and foreign protein therapy.

Blastomycetic Dermatitis. Presented by Dr. G. W. Binkley.

W. M., a Negro aged 56, from the service of Drs. Cole and Driver at the Cleveland City Hospital, complains that a "pimple" developed on the right side of his neck about one year ago, while he was cleaning out a creek bed on a WPA project. The lesion gradually became larger, until at present it measures 2½ by 6 inches (6 by 15 cm.) and covers the under-surface of the jaw and the right side of the neck. The borders are sharply defined, raised and verrucous, and the surface of the lesion presents numerous miliary pustules.

A roentgenogram of the chest showed healed tuberculosis and silicosis. The aorta was widened, and the Wassermann and microscopic precipitation tests of the blood were strongly positive. Direct smears from the pustules revealed budding yeastlike organisms.

Histologic examination showed marked irregular acanthosis of the epithelium, especially near the pustules. Under the epithelium were collections of all types of leukocytes in a massive infiltration. In places the infiltration was almost purely polymorphonuclear, and in such areas giant cells and an occasional yeastlike cell were found.

DISCUSSION

DR. H. N. COLE: The condition clinically is a classic example of blastomycosis, and the case is presented because of the rarity of this disease in the Cleveland district. This is the first case that my associates and I have observed in at least three years. It is interesting to note that in the Chicago area such cases are not uncommon. The reason for this I do not understand.

LOS ANGELES DERMATOLOGICAL SOCIETY

HARRY P. JACOBSON, M.D., *President*

Feb. 9, 1937

THOMAS W. NISBET, M.D., *Secretary*

Scleroderma and Sclerodactylia Associated with Intermittent Claudication.
Presented by DR. SAUL S. ROBINSON.

C. B., a white married man aged 56, noticed about ten years ago that his fingertips were cold to the touch and that at the tips of several fingers there developed calluses, which disappeared after a short time. During the past year, the skin on the fingers has become thickened, hard, rigid and bluish white. About six weeks before he consulted me, the patient filed the nails of his right hand, and the index and middle fingers became infected. Under the nail beds of these two fingers appeared painful, slow, indolent ulcers, which were stubborn in healing. The fingertips have been cold to the touch. During the past few months severe pain has been felt in the lower part of the right leg during walking, which has necessitated rest before walking could be continued.

Examination reveals induration and thickening of the skin of the fingers, with healed trophic ulcers at the tips of several fingers. There is a tender dime-sized ulcer on the right heel. Pulsations are absent in the ulnar arteries at both wrists, the right popliteal artery, the right posterior tibial artery and the right dorsalis pedis artery. There is marked pallor on elevation of the right foot, and rubor is noted on dependency.

The complete blood count gave normal results. The Kolmer and Kahn serologic reactions were negative. The vasomotor index with alcohol showed a rise in the left fingers to 35 C., in the right fingers to 34.5 C., in the left toes to 33 C. and in the right toes to 29 C. Exposure of the hands to heat or their immersion in hot water helped to raise the surface temperature only temporarily. The claudication time on exercise (walking) was two minutes and forty seconds. It is now six minutes.

DISCUSSION

DR. SAUL S. ROBINSON: The interesting point in this case is the association of intermittent claudication with scleroderma and sclerodactylia. The intermittent claudication here is due to arteriosclerosis obliterans. I would like to bring out the fact that this patient was told to stop smoking or to smoke so-called denico-

tinized cigarets, and it has been found that he gets practically the same lowering of the vasomotor index with alcohol when denicotinized cigarets are used as he did when regular cigarets were consumed.

DR. HARRY P. JACOBSON: I wish to go on record with an opinion somewhat at variance with that which has been offered. I readily concede that this patient presents characteristic sclerodactylia, but I fail to see any evidence of scleroderma. My conception of sclerodactylia is that it is a cutaneous expression of a trophovascular disturbance involving usually the fingers, occasionally the feet and rarely the face. The history given by the patient and Dr. Robinson, together with the clinical picture, is in my opinion that of sclerodactylia, although without any concomitant scleroderma.

Basal Cell Epithelioma of the Neck, Possibly Overlying Lupus Erythematosus; Basal Cell Epithelioma of the Nose. Presented by DR. ANKER K. JENSEN (by invitation) for DR. FREDERICK NICHOLS.

W. P., an American woman aged 60, is a teacher. In 1917 she noticed a number of slightly elevated red lesions, varying in size from that of a match head to that of a dime, situated on the forehead and the left side of the neck. In 1919 the patient had a paste applied to these lesions. There is a dime-sized scar on the forehead from the paste. The lesion on the neck did not clear up completely, and in 1927 the patient received five treatments with roentgen rays. The lesion on the side of the neck is palm-sized, with a slightly raised circinate border and some crusting. In its center scar tissue, probably due to the paste, is present. The lesion on the side of the neck is gradually getting larger. Parts of the border are suggestive of carcinoma. The roentgen radiation did not relieve the condition. How much therapy the patient received is unknown. A biopsy specimen was taken from the margin of one of the suspected areas; the pathologist reported that the section presented a picture compatible with a diagnosis of early cancer. The Wassermann reaction of the blood was negative.

The lesion on the nose was electrodesiccated.

DISCUSSION

DR. STANLEY CHAMBERS: It would have been interesting to see the original clinical lesion and watch it through its developmental phases. The presence of true lupus erythematosus cannot be denied in the interpretation of the clinical picture at this time. That malignant degeneration has subsequently developed in isolated portions of the area affected by lupus erythematosus is unquestioned.

DR. J. C. HATHAWAY (by invitation): The clinical picture suggests basal cell epithelioma superimposed on long-standing lupus erythematosus. After seeing the patient I went back and looked at the section again, but it did not show enough to bear out the clinical impression.

DR. C. R. HALLORAN: I also thought that the epitheliomas were superimposed. The lesion on the neck impresses me as lupus vulgaris.

DR. SAUL S. ROBINSON: If this condition proves to be basal cell epithelioma of the multiple type, I want to make a suggestion, as I have recently treated a patient for a similar condition, and roentgen rays did not seem to stop the recurrence. The only thing that seemed to cure the areas was removal of the lesions by the Post cautery. I kept the patient under observation during the past two years, and in the area treated with roentgen rays the condition seemed to recur, whereas in areas treated by cautery there seemed to be no recurrence.

DR. CHARLES R. CASKEY: I had an experience similar to that of Dr. Robinson, except that I used radium instead of roentgen rays in lupus erythematosus with epitheliomatous changes. The lesions did not respond well to the irradiation. I think the cautery is better.

DR. HARRY P. JACOBSON: I agree with what Dr. Chambers said regarding the character of the primary lesion of the neck. The impression one gets is that this lesion is old lupus erythematosus. The lower portion presents two well defined, sharply marginated patches with fairly suggestive borders and a good deal of characteristic infiltration. These undoubtedly are malignant, and the treatment of choice is excision by cautery.

Keratosis Follicularis (Darier) in Mother and Child. Presented by DR. H. S. CAMPBELL.

This woman, aged 40, says that an eruption first appeared in 1917 between the fingers and on the dorsa of the hands. Later the palms and soles became markedly thickened. The neck and the abdomen were next involved. All lesions were cleared up in about six months by Dr. G. F. Koetter, who treated them with sodium iodide. The condition recurred the next year, and there was no response to similar treatment. The condition has shown response to treatment with thyroid, sodium iodide and calcium.

The patient's son, aged 6½ years, demonstrates lesions over the dorsa of both hands, with some commencing papules on the palms. These first appeared when he was 6 years old. The first biopsy specimen was taken from the palm, but the section proved to be too superficial, little but hyperkeratoses being demonstrated, though even at that level *corps ronds* could be seen in the substance of the markedly thickened corneous layer. The next section manifested only the feature emphasized by Weidman, namely, interpapillary cyst formation. Four sections in all were taken before typical cyst formation containing round bodies was found.

DISCUSSION

DR. NELSON PAUL ANDERSON: As Dr. Hathaway remarked, how many dermatologists would make a diagnosis of Darier's disease in the child in the absence of the disease in the mother?

MANHATTAN DERMATOLOGIC SOCIETY

ISADORE ROSEN, M.D., *Chairman*

March 9, 1937

MIHRAN B. PAROUNAGIAN, M.D., *Secretary*

Lupus Erythematosus Disseminatus. Presented by DR. GEORGE C. ANDREWS.

J. H., a woman aged 48, suffered from characteristic lesions of lupus erythematosus on the cheeks after excessive exposure to the sun in 1934. These disappeared after injections of a gold preparation, but last year another attack occurred, and the lesions on the face and the neck did not respond to injections of sodium gold thiosulfate. The patient was operated on in 1930 for appendicitis, tuberculosis of the mesenteric glands and cystic ovary. She recently went to Florida, where, although she was exposed as little as possible to the sun, her condition has grown much worse and has spread to the dorsa of the hands, the forearms, the neck and the cheeks. She is being treated by injections of a bismuth preparation and extract of liver.

DISCUSSION

DR. ISADORE ROSEN: When bismuth is used in the treatment of lupus erythematosus, at least three or four courses must be given, as in syphilis, to obtain the desired effect. The reason the results have not been satisfactory is because the treatment was not continued long enough.

DR. GEORGE C. ANDREWS: The important point in this case is the sensitivity to light. I think injections of liver have been beneficial. Excretion of porphyrin is high in most patients with sensitivity to light. The benefits of extract of liver and the Sauerbruch diet may be explained by their action on hepatic function and the production of porphyrin.

Pemphigus Vulgaris. Presented by DR. LUDWIG OULMANN.

M. M., a woman aged 75, in June 1936 suffered from the development of blisters over the entire body with the exception of the mucous membranes. These blisters arose mostly on the normal skin, but there was also an erythematous urticarial eruption. The patient grew weaker and had to stay in bed. With a diet high in vitamins and administration of arsenic she recuperated, so that by September she was able to be up. From September to November there were no lesions. In November new lesions developed, first on one breast and then on the other, followed by further eruptions on the four extremities and later on the chin and the neck. The eruption on the extremities appears as gyrate patches of erythema with vesicles at the margin. The iodide test gave negative results. There is not much pruritus. The patient is in fairly good health. Owing to albuminuria, treatment with germanin was not considered suitable.

DISCUSSION

DR. MIHRAN B. PAROUNAGIAN: I am inclined to the diagnosis of dermatitis herpetiformis for the following reasons: absence of lesions of the mucous membranes, distribution (knees and buttocks), hemorrhagic vesicles and lesions with peculiar configuration, the borders being studded with vesicles.

DR. HOWARD FOX: I disagree with the diagnosis of pemphigus. The fact that the eruption appeared suddenly and cleared up entirely for a few months does not suggest pemphigus. Furthermore, the patient is rather old for that disease and has not had any lesions in the mouth. There is considerable itching, which is strongly against a diagnosis of pemphigus, and there are numerous reddish firm dry papules on the forearms, which are not part of the picture of pemphigus. This condition, I think, is probably a toxic eruption which was bullous at the outset and is now of a rather persistent erythematopapular type.

DR. JEROME KINGSBURY: I do not regard the condition as pemphigus. I agree with much of what Dr. Fox has said.

DR. LUDWIG OULMANN: When I saw the patient last summer she was almost moribund. With a diet high in vitamins, together with administration of iron and arsenical preparations, she recuperated. The large blisters at that time would have been diagnosed as pemphigus by any dermatologist. The present lesions have improved much under ultraviolet irradiation, in addition to the general treatment. The iodide test gave negative results, which speaks against the diagnosis of Duhring's disease.

Pustular Bacterid. Presented by DR. GEORGE C. ANDREWS.

D. H., a woman aged 32, presents an eruption which developed simultaneously on the palms and the soles one year ago as multiple pinhead-sized vesicopustules. The fingers and toes have remained free. She was treated by another physician with roentgen rays and compound ointment of benzoic acid N. F. When seen three months ago, she was found to have large, inflamed and cystic tonsils, and congestion of the pharynx. A tonsillectomy was performed on January 7. Improvement began after this operation and has continued. When last seen ten days ago, she had only a few vesicles. There were also some hyperkeratotic scales on the soles over points of pressure. Histologic examination failed to show psoriasis.

DISCUSSION

DR. LUDWIG OULMANN: Since Dr. Andrews reported on the subject in Chicago, I am of the opinion that pustular dermatitis of the hands and soles and psoriasis pustulosa are two different diseases. As far as I am informed, Dr. Barber himself agrees with this view.

DR. FRED WISE: I think it is not practical to make a diagnosis before a long period of observation. One histologic examination is not enough to rule out psoriasis.

DR. ISADORE ROSEN: I believe that this patient has pustular psoriasis, despite the fact that the microscopic findings do not verify the diagnosis. Often, on account of the variety of treatment instituted in such conditions, the clinical features change, and therefore the histologic picture will fail to show the characteristic morphologic picture. This patient has a glazed, sharply outlined micaceous scaly lesion on the ankle, which speaks for psoriasis.

DR. GEORGE C. ANDREWS: In the cases I have presented I did not find much evidence of acute, inflammatory dermatitis. Indeed, one remarkable characteristic has been the paucity of inflammation. One characteristic of the microscopic picture is its resemblance to trichophytid. Clinically, one should have the essential lesion of psoriasis—an erythematous papule with micaceous scales—to make a diagnosis of that disease. Without it and without a history or microscopic evidence of psoriasis such a diagnosis is untenable.

A Case for Diagnosis (Lichen Simplex Chronicus. Trichophytid?). Presented by DR. GEORGE C. ANDREWS.

E. C. P., a man aged 53, presents a lesion on his left calf, which developed seventeen years ago as a moist, itching eczematous eruption. It persisted for years and cleared up during an attack of pneumonia, but recurred eight months later as an infiltrated bluish red plaque. The surface is dry and smooth. Palpation at the border elicits infiltration. The patient also has vesicular eruptions on the backs of the fingers. These lesions have recurred at intervals for fifteen years or more. Recently his fingernails became disfigured. Scrapings from his nails showed no fungus.

DISCUSSION

DR. FRED WISE: The lesion on the leg would be diagnosed as lichen simplex by everybody. Freudenthal has described a similar condition which proved to be amyloid degeneration of the skin. Whether the lesions on the hands are related to the lesion on the leg I could not say. I will qualify my discussion by saying that the patch on the leg did not have the usual shagreen-like changes, nor the crisscross peculiar to lichen simplex chronicus (Vidal); but it looked somewhat like amyloid degeneration. I merely offer that as a suggestion.

DR. HOWARD FOX: I should like to ask Dr. Wise whether he suspects amyloidosis and tests for its presence in every similar case of lichen simplex chronicus.

DR. GEORGE C. ANDREWS: I presented this case because my associates and I felt that the condition did not look like ordinary lichen simplex chronicus. There are few epidermal changes in this patch. It seems to be, rather, an infiltration of the skin.

Recurrent Chronic Erysipelas with Persistent Lymphedema. Presented by DR. GEORGE C. ANDREWS.

A. M. F., a woman aged 43, says she first noticed cutaneous trouble in Guatemala five years ago, when she awoke one morning with her face badly swollen and her eyelids completely closed by edema. This condition was diagnosed as onchocerciasis by Sir Aldo Castellani, who gave injections which caused the condition to disappear rapidly. There have been no visual disturbances or edema since that

time. About one year ago the patient began having sties, and this condition was followed by a swelling of the left side of the face. The swelling has been recurrent during the past several months and has at times been accompanied with malaise and mild fever. Roentgenograms of the sinuses and the teeth showed no signs of focal infection. The patient was recently seen by Dr. Castellani, who agreed that the present condition has no relation to the previous filarial infection and is a form of chronic recurrent erysipelas. The reaction to streptococcus toxin was positive. The patient is being treated by injections of this toxin and by fractional (75 roentgen) doses of roentgen radiation.

DISCUSSION

DR. HOWARD FOX: I believe the diagnosis made by Sir Aldo Castellani in this case is correct, namely onchocerciasis, locally called *erysipela de la costa*. It is a coincidence that I am seeing this patient about a week after my return from Guatemala, where the disease is endemic. While onchocerciasis is most prevalent in Guatemala, cases are also observed in other countries of Central America. The patient gave a history of numerous bites from flies. (A species of Simulium is thought to be the usual vector of the parasite.) She stated that after these bites her entire face became red and extremely swollen, the eyes being closed for a time from edema. Associated with this eruption were various febrile symptoms. I think this was undoubtedly onchocerciasis.

There are several features of dermatologic interest in this tropical disease, the first being the erysipelatous eruption associated with severe edema. Later, cysts of cartilaginous hardness develop on various parts of the body, notably the scalp and the face. These contain the microfilarias, which escape and invade the surrounding apparently normal skin. Surgical removal of these cysts often causes rapid and striking amelioration in vision, which is the most serious feature of the disease. I was told by Dr. Robles, after whom the disease is often called, that there were a thousand or more persons in Guatemala who were permanently blind as a result of this disease.

Other features of interest to the dermatologist are the peculiar greenish hue of the face when the condition is chronic and, particularly, the striking dermographism that is usually present. In many cases stroking of the skin is followed by urticarial wheals which remain for from one to two hours. I saw such a reaction in a patient who had first been infested twenty years previously. I was also interested in the demonstration of microfilarias in a tiny piece of tissue snipped from the neck of a man who had suffered from onchocerciasis for seven years. The only clinical symptom he presented at the time was the peculiar greenish color of the cheeks.

Acrodermatitis Perstans (Hallopeau). Presented by DR. J. FRANK FRASER.

M. H., a white girl aged 20, entered the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 6, 1937, complaining of an eruption on the right thumb of twelve years' duration. The lesions consisted of vesicles, pustules, scaling and fissures. The nail was thickened and dystrophic. There was no other involvement except a small fissure in the fourth interdigital space of each foot. Roentgenograms showed no abnormality, and the Wassermann reaction was negative. There was no history of injury. Intradermal tests with 0.1 cc. of a 1:100 dilution of oidiomycin showed erythema with 1 cm. of infiltration. Tests with 0.1 cc. of a 1:30 dilution of trichophytin and with 0.1 cc. of staphylococcus toxin (Hopkins)) and patch tests with oidiomycin and trichophytin, undiluted, gave negative results. The treatment consisted of ten exposures to roentgen rays two years ago at the Presbyterian Hospital. The nail was removed surgically four times.

DISCUSSION

(There was unanimous agreement in the diagnosis.)

Pityriasis Lichenoides et Varioliformis Acuta in a Boy Aged 5 Years. Presented by DR. PAUL E. BECHET.

M. W., a boy aged 5 years, has had an eruption on his arms and legs for eight weeks. It began as a vesicular outbreak and, despite absence of constitutional symptoms and of any rash on the trunk, was diagnosed as varicella. Instead of clearing up in the usual interval, the eruption has become progressively worse. The patient's general health is good, and no drug other than castor oil has been taken. On the arms, the face, the legs and the hands are lesions, varying in color from yellowish to red and in diameter from 1 to 2 mm. The newer vesicles are distinctly inflammatory, and the older ones are topped by a yellowish crust. The papules are scaly and characteristic of a guttate parapsoriasis. A histologic examination confirmed the clinical diagnosis.

DISCUSSION

DR. LUDWIG OULMANN: When Habermann published reports of his cases of pityriasis lichenoides et varioliformis acuta, he called it "acuta" because in his cases the condition cleared up. I have observed a number of such eruptions which disappeared entirely, as most of the members have. Some eruptions may leave tiny scars, and others may persist and become chronic.

DR. FRED WISE: I believe the prognosis of the varioliform type of parapsoriasis is variable. In some cases recovery is spontaneous in a few weeks; in others the condition responds to massive doses of ultraviolet radiation; in still others the condition is recalcitrant to most remedies and appears to become chronic.

Congenital Ectodermal Defect. Presented by DR. GEORGE C. ANDREWS.

C. R., a man aged 28, was previously presented at the meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine on Oct. 3, 1922, at about the age of 14 (ARCH. DERMAT. & SYPH. **7**:250 [Feb.] 1923; **10**:676-689 [Dec.] 1924).

DISCUSSION

DR. GEORGE C. ANDREWS: I am pleased with the patient's good mental development. He has certainly overcome a great many defects. He is getting his degree in chemistry from New York University next fall.

Porokeratosis (Mibelli), Disseminated and Superficial Type. Presented by DR. GEORGE C. ANDREWS.

M. St. J., a girl aged 14, has an eruption that began eleven years ago, and now there is extensive involvement of the legs, the axillae, the shoulders and the back. The lesions are festooned, lobulated and rounded patches with slightly atrophic centers, surrounded in some places by a definite corneous ridge. Histologically there was marked hyperkeratosis and acanthosis, with elongation of the rete pegs. Some parakeratosis was present, being most pronounced about the outlets of the coil gland. In other parts of the epidermis there was distinct atrophy, with loss of rete pegs. The corium was the site of a chronic inflammatory reaction, associated with thickening of the walls of the blood vessels, edema, and an infiltration that contained numerous mast cells. The basal metabolic rate was minus 8 per cent. The blood count and chemical tests of the blood gave results within normal limits.

DISCUSSION

DR. FRED WISE: Instances of the disseminated, superficial variety of porokeratosis (Mibelli) have recently been described in two or three Italian publications. The clinical descriptions of the lesions correspond to the picture present in this case. Abstracts may be found in the "Year Book of Dermatology and Syphilology" (Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1934, pp. 253-254).

A Case for Diagnosis (Chronic Eczema?). Presented by Dr. J. Frank Fraser.

L. H., a Negro aged 35, born in the United States, was first seen on Nov. 1, 1935, when a tentative diagnosis of tinea was made. On Feb. 25, 1937, the patient was seen again, on which occasion he presented well defined patches on the arms and forearms. The patches show areas of vesiculation with central lichenification and scaling. The Wassermann test and the examination for tinea gave negative results. The histologic picture was that of chronic eczema.

DISCUSSION

Dr. Howard Fox: I think this is undoubtedly a case of the eczematoid type of ringworm, a condition formerly called parasitic eczema. The sharp demarcation of the patches and the presence of a vesicular border, with some itching and oozing, favor this diagnosis. The scaling is not of the type that occurs in psoriasis, even though that disease is occasionally seen in full-blooded Negroes.

Pustular Bacterid. Presented by Dr. George C. Andrews.

F. M. S., a man aged 39, has an eruption that began with an outbreak of pinhead-sized vesicles on the palms in December 1935. He was treated at the time with local remedies for tinea. When he was first seen by the presenter, both palms were covered with small vesicopustules. The same condition later developed on the soles and on the sides of the feet. Microscopic examination and cultures of material from the lesions for fungi have repeatedly given negative results. The patient has one enlarged and apparently infected tonsil. The other was removed twenty years ago. The eruption did not respond to roentgen radiation.

DISCUSSION

Dr. Anthony C. Cipollaro: It seems to me that pustular psoriasis of Barber and pustular bacterids of the palms and soles described by Andrews are clinically the same. Pustular psoriasis need not be accompanied by psoriasis vulgaris elsewhere. The response following removal of foci of infection does not serve to differentiate these two conditions. Again, psoriasis associated with pyoderma is not the condition described by Barber as pustular psoriasis. The case presented by Dr. Andrews is, in my opinion, one of pustular psoriasis. The clinical picture fits in exactly with that of Barber's disease. The changes in the nails of this patient are those of ordinary psoriasis.

Dr. George C. Andrews: Dr. Barber wrote to me recently that he is publishing an article on pustular bacterid in the *British Journal of Dermatology and Syphilis*. He feels that the condition is different from pustular psoriasis. No one in this man's family has psoriasis. I have been studying his condition for two years, and he has never shown any signs of psoriasis. He has severe pansinusitis and a chronic hypertrophic tonsil, but it is impossible to operate on him because he is a bleeder. He has seen several otolaryngologists, who concur in this opinion.

A Case for Diagnosis (Alopecia Areata? Monilethrix?). Presented by Dr. George C. Andrews.

A. D., a Negress aged 57, presents loss of hair and itching of the scalp of nine years' duration. The crown of the scalp is bald, except that there are short broken-off, thickened hairs over the entire area. There is mild inflammation about the follicles but no atrophy. The menopause began about fifteen years ago, after removal of an ovarian cyst. Microscopic examination showed no fungi, but there are constricted areas about the hairs like those seen in monilethrix.

DISCUSSION

DR. HOWARD FOX: It is difficult to name this peculiar eruption. It is certainly not alopecia areata. It cannot be considered to be monilethrix, as there are no beaded hairs. The process is universal and of comparatively recent date. It would appear to be alopecia due to some unusual type of folliculitis. I would not class this as folliculitis decalvans, as that disease rarely if ever causes complete loss of hair. Furthermore, the scalp is not sclerotic, as in that condition.

DR. H. BROOKS (by invitation): There have been cases of lichen planus reported in which there are associated patchy alopecia of the scalp and follicular keratoses, so-called lichen planopilaris. I thought of that disease in conjunction with this case, and I suggest that it be kept in mind in examining patients with complaints of this type.

BRONX DERMATOLOGICAL SOCIETY

PAUL GROSS, M.D., *President*

March 25, 1937

HENRY SILVER, M.D., *Secretary*

Anetoderma of Jadassohn. Presented by DR. SAMUEL FELDMAN.

I. S., a man aged 56, states that about four years ago he noticed spots on the thighs and that since that time the lesions have increased in size and in number. On the buttocks and the upper portions of the thighs there are about forty lesions of somewhat varied appearance. On the inner surface of the upper portion of the thigh there is a white oblong lesion the size of a 5 cent piece. The surface is wrinkled and ballooned and has a soft and easily compressible center and firm edges. On the buttocks, on the upper aspects of the thighs and in the lumbar region there are a number of sharply defined brownish round or oval wrinkled lesions. They are slightly elevated and somewhat firm, particularly in the center. A few lesions the size of a dime or smaller show mottled surfaces; the color alternates between brownish and distinctly red, the latter hue probably caused by dilated capillaries and minute hemorrhages.

A comparatively large number of lesions, usually round and not larger than a pea or a lentil, show an exaggerated wrinkling of the surface. They are elevated and baggy and give the appearance of blebs the contents of which have been emptied. On being stretched, the surface of the skin remains deeply wrinkled. The lesions give the impression of complete loss of elasticity and can be stretched to several times their natural dimensions. On the glans penis there are a few firm lesions which, the patient states, have been present for over twenty years. They are deeply embedded in the structure of the glans and resemble lipomas or fibromas.

The histologic examination showed that the rete consisted of from five to six layers and was slightly swollen and edematous. The basal cell layer contained an excessive amount of pigment. There was an obliteration of the papillae and the interpapillary pegs. The cutis was edematous. The collagenous bundles were edematous, swollen and separated from one another. Cellular elements were not abundant and were situated mostly in the vicinity of the blood vessels. Most of the cutis showed a basophilic staining of the collagen. The blood vessels were dilated. The section from a tumor-like lesion on the penis showed essentially the same structure as did that from the atrophic lesion, except that the collagenous bundles were coarser and packed more closely and there was marked dilatation of the lymphatic spaces. The Weigert stain disclosed a marked diminution and disappearance of the elastic tissue. The areas in which elastic fibers were still

present corresponded almost exactly to the areas in which the collagen retained the acidophilic (fuchsin) staining. Even in these areas the elastic fibers were coarse and broken up into short thick shreds and coarse granules. Both sections showed identical changes of the elastica. The Van Gieson stain turned most of the collagen brownish yellow, and only isolated areas stained red with fuchsin. The acid orcein-polychrome methylene blue stain showed, in addition to the partial disappearance of the elastic tissue, the blue staining of the remnants of the elastic tissue and also of large areas of collagen.

Syphilitic Macular Atrophy of the Skin. Presented by DR. MARION B. SULZBERGER.

A. K., a painter aged 57, born in Russia, has resided in the United States for the past fifty-one years. In 1890 he had favus of the scalp, and in 1926, pulmonary tuberculosis. In 1922 he acquired a penile sore, which was followed by an eruption on the trunk and the arms. Soon after the disappearance of that eruption the patient noticed cutaneous lesions which have persisted till the present time. The first Wassermann test of the blood, done in 1926, gave a 4 plus reaction. Aside from a few injections of bismuth subsalicylate in 1933 the patient has received no treatment.

The scalp shows large, irregularly shaped bald areas with slight depigmentation and follicular atrophy. The eruption covers the trunk (with the exception of the lower part of the chest and the abdomen), the arms and the upper third of each thigh. On the back the lesions are arranged along the lines of cleavage. The lesions are oval, atrophic and the color of normal skin. They vary in size from that of a bean to that of a coin, and most of them protrude slightly above the level of the skin. The majority of the lesions are soft; others are fairly firm. Many show marked wrinkling of the surface of the skin. On the dorsum of the shaft of the penis there is a superficial scar, the site of the primary sore.

The Wassermann reaction of the blood was 3 plus. The Wassermann reaction of the spinal fluid was reported negative in 1932. (The patient is under the care of Dr. R. Baer.)

DISCUSSION

DR. LOUIS CHARGIN: One encounters rather infrequently cases of true anetoderma of Jadassohn. I recall but one case, and in that instance the condition did not resemble in all details that of the patient presented this evening. Since the clinical manifestations in this patient cannot be fitted into the picture of any of the diseases that are known to be followed by so-called secondary macular atrophy, the case must be regarded as an unusual one of the primary variety. There are two types of primary macular atrophy, that of Jadassohn and that of Schweninger and Buzzi, and the manifestations in this patient, even if they do not correspond to the original description, must be looked on as those of anetoderma of Jadassohn.

DR. SAMUEL FELDMAN: Careful investigation did not reveal any condition which could account for the macular atrophy. I had the good fortune to observe the progress of a single lesion from its onset to the development of atrophy. This lesion, located on the anterior aspect of the left thigh, began as an erythematous macule which in a comparatively short time showed the features of atrophy, such as wrinkling and herniation. On the glans penis there are three hard noduar lesions which one would hardly suspect, clinically, of being atrophic; yet under the microscope the lesions are identical with those which show definite atrophy. There is marked edema, and the elastic tissue is, for the most part, missing. The remnants of the elastic tissue show the various stages of degeneration. Wherever the elastic tissue is missing, the collagen also shows tinctorial changes, and where some elastic fibers are still present, the collagen possesses better staining qualities.

DR. WILBERT SACHS: As far as I recall, the collagen is not affected, and there is basophilic degeneration in macular atrophy. I suggest that a piece of normal skin be examined.

DR. MARION B. SULZBERGER: There is no proof that the atrophoderma in my case is really secondary to syphilis. I do not believe that there is any way of proving the causal connection, but the distribution and the man's history suggest that this macular atrophy is probably secondary to syphilis.

DR. HENRY SILVER: I am inclined to agree with Dr. Sulzberger's remarks regarding his case. It is extremely difficult to prove whether the atrophy is primary or secondary unless one is fortunate enough to observe the actual course of the case from the beginning. If one observes the transition of a syphilitic lesion to macular atrophy, one can say with certainty that the condition is secondary macular atrophy. But it must be remembered that syphilis and primary macular atrophy may coexist and that the anetoderma is then more frequently of the type of Schweninger and Buzzi.

I agree with Dr. Chargin that a simplified classification of the macular atrophies is necessary. In the absence of known etiologic factors, classification must necessarily be made on purely clinical and histologic grounds. The insistence on primary and secondary atrophies is helpful and will remain so until more is known about the etiology.

It is to Dr. Feldman's credit that he correctly diagnosed the condition in his case as anetoderma of Jadassohn. This type presents always a diagnostic problem, because of the varied clinical picture. The lesions may be located anywhere on the body, and when, as is the rule, they appear on the face, it is difficult to rule out lupus erythematosus in the early stages. In typical eruptions there are red macules or papules, sharply defined and growing peripherally, until after a few months they clear in the center, become pale and wrinkled and form a reddish ring. In the last stage there is a slightly depressed smooth, whitish spot or an elevated, ballooned skin-colored lesion, almost always showing herniation.

Lichen Sclerosus et Atrophicus. Presented by DR. DAVID BLOOM.

G. F., a Ukrainian woman aged 59, was presented before the New York Dermatological Society on Oct. 27, 1936 (ARCH. DERMAT. & SYPH. **35**:1200 [June] 1937).

The eruption has not changed much during the past year.

A recent histologic examination of a section taken from a small plaque revealed atrophy of the superficial epithelium and sclerosis and hyalinization of the immediately underlying connective tissue, in which were scattered islands of round cells, most of them being lymphocytic.

DISCUSSION

DR. SAMUEL FELDMAN: There is one typical feature of lichen sclerosus, namely, the dilated follicles and plugs. One can see that the patches are made up of individual papules which have fused. There is no question that this case is one of lichen sclerosus.

DR. MARION B. SULZBERGER: Is lichen sclerosus considered to be a form of lichen planus or a separate clinical entity?

DR. DAVID BLOOM: With regard to Dr. Sulzberger's question, there is marked dissension in the opinions expressed in the literature. When I first saw this patient I thought of lichen planus, because there were discrete shiny violaceous, umbilicated papules. The ivory white color of other papules suggested sclerosis, and the yellowish, wrinkling surface of several plaques suggested atrophy. Thus, the description fits the diagnosis of lichen sclerosus et atrophicus.

DR. SAMUEL FELDMAN: Lichen sclerosus is generally accepted as a separate entity. In my paper on lichen planus et acuminatus atrophicans (ARCH. DERMAT. & SYPH. **5**:102-113 [Jan.] 1922) I advanced the view that there is some relation between all the atrophic forms of lichen and lichen planus. The former are linked to one another by one common feature, namely, the presence of the horny plug or of the dilated follicle which follows the falling out of the plug. This feature is pathognomonic of lichen sclerosus. Similar conditions which are described under various names are linked to lichen planus by the fact that many of them begin

with a chromatic papule of lichen planus, which later becomes white. This was the condition in several of Hallopeau's patients. Even when the papule is white from the start, the lesion may be a modified lesion of lichen planus. Differences in the clinical appearance of the lesions in different cases have occasioned classification of the condition under various names, but the differences merely represent various stages of the same disease. Microscopically, this condition differs from lichen planus by the presence of infiltrate in the middle portion of the cutis instead of just under the epidermis, as is characteristic of lichen planus. Darier pointed out the possibility that sclerosis causes displacement of the infiltrate downward and its disappearance from the usual location. This has apparently been demonstrated by later observers.

DR. WILBERT SACHS: The pathologic picture of lichen sclerosus is similar to that of lichen planus, with some variations. The epidermis is thin rather than acanthotic, and there is sclerosis between the epidermis and the bandlike cellular infiltrate.

DR. ARTHUR SAYER: I suggest that several biopsy specimens be taken from the various types of lesions. I stress this, in view of a recent report of a case of lichen ruber moniliformis by Drs. Wise and Rein (ARCH. DERMAT. & SYPH. **34**: 830 [Nov.] 1936). You will recall that eleven specimens were obtained in that case before the authors came to the conclusion that the condition was a separate entity and not a variant of lichen planus. The patient presented has certain lesions on the neck which are violaceous, flat-topped and shiny and which, taken by themselves, suggest lichen planus. The other lesions on the body are whitish and somewhat atrophic and conform rather to the clinical appearance of lichen sclerosus et atrophicus.

DR. DAVID BLOOM: Tissue was taken from a small patch formed by confluence of several papules. The microscopic examination failed to show the pathologic picture of lichen planus. The patient has had this eruption for over one year, and it is entirely possible that the pathologic picture has changed.

A Case for Diagnosis (Angiolupoid?). Presented by DR. MARION B. SULZBERGER.

Mrs. R. I., a housewife aged 54, born in Bulgaria, has resided in the United States for the past two and one-half years. About twenty-five years ago she had pneumonia, and about ten years ago, typhoid. About one and one-half years ago a lesion developed on the nose, which apparently did not enlarge.

On the upper part of the right side of the nose there is an oval lesion about 2 cm. in diameter, which is slightly raised above the level of the surrounding skin and which is fairly soft. The color of the lesion is dark red. A few telangiectases are seen in the peripheral parts, and on pressure a yellowish tint is observed. There is no scaling or atrophy.

A tuberculin test with a 1:10,000 dilution gave a weakly positive result. Roentgen examination of the chest revealed no abnormality in the lungs. The nodes at both hili showed some enlargement and calcification. There was evidence of an old fracture of the styloid process of the right ulna. In the left hand complete fusion of all the carpal bones with the lower end of the radius, as well as with the second metacarpal bone, was evident. There were marked changes of osteo-arthritis about the big toe of the right foot. The lesion was most marked in the distal third of the first metatarsal bone. (The patient is under the care of Dr. R. Baer.)

DISCUSSION

DR. WILBERT SACHS: I think that a microscopic examination will rule out lupus erythematosus but will not establish a definite diagnosis.

DR. MARION B. SULZBERGER: The localization and the appearance of the lesion and the sex and the age of the patient all suggest angiolupoid. This lesion has no feature that would enable one to make a diagnosis of lupus erythematosus, and

it presents more dilated blood vessels than one usually sees in ordinary sarcoid. The affected area will have to be excised in toto, and histologic examinations will have to be made.

Lupus Erythematosus or Sarcoid. Presented by DR. DAVID BLOOM.

F. S., a woman aged 56, presents a lesion the size of a 5 cent piece on the bridge of the nose. It consists of a central elevation, resembling a fleshy mole, surrounded by a round erythematous areola with a slight uneven infiltration. The central portion persisted for many years, while the erythematous zone appeared one year ago.

The Wassermann reaction of the blood was negative. The tuberculin test with a 1 : 1,000,000 dilution gave a negative reaction; that with a 1 : 100,000 dilution, a moderately positive reaction, and that with a 1 : 10,000 dilution a strongly positive reaction.

The histologic examination of the erythematous area revealed numerous vacuolated cells, with regular patches of spongiosis and colliquative degeneration in the epidermis. In some planes the rete was slightly thin. The corium contained numerous cross-sections of hair follicles and areas of perivascular and perifollicular infiltration, areas of the former predominating. The infiltration contained round cells and a few plasma cells, and in some foci there were many eosinophils. Marked edema of the collagen was noted.

DISCUSSION

DR. FRANK E. CROSS: It will be noticed that the lesion is located on the bridge of the nose, and any lesion over a bony surface is exaggerated and has a tendency to change of color. One must take the location into consideration in evaluating the diagnosis. This, in conjunction with the telangiectasia and the duration, makes the diagnosis of sarcoid acceptable.

Prurigo Nodularis. Presented by DR. SAMUEL FELDMAN.

S. C., a housewife aged 60, born in Russia, states that two nodules appeared on the extremities about fifteen years ago. They itched and annoyed her considerably. Other lesions appeared gradually over the course of many years. None of the lesions has disappeared during all this time. On the contrary, they gradually have become larger and firmer.

A comparatively large number of nodules are seen, mostly on the posterior surfaces of the forearms and arms, about the elbow and the dorsa of the hands and on the anterior surfaces of the legs and knees. On one upper extremity there are about thirty lesions. Each lesion is discrete, elevated and hemispherical, with a rough and in some instances almost verrucous surface. There are marked hyperkeratosis and scaling. Most lesions are excoriated at the apex, owing to scratching. The lesions are hard and range in size from that of a small pea to 0.5 cm. in diameter.

The blood count, the estimation of hemoglobin, the urinalysis and the chemical examination of the blood gave normal results. The Wassermann reaction was negative.

The microscopic examination showed a marked hyperkeratosis but no parakeratosis. The granular layer was well defined, and the rete pegs were considerably elongated. There was mild edema of the rete. The papillae were enormously elongated; in some areas they projected above the surface, giving it an irregular, verrucous outline. The collagenous bundles were thickened and separated by edema. The blood vessels and lymphatics were dilated and surrounded by almost solid masses of infiltration, consisting of lymphocytes, plasma cells and fibroblasts. Several eosinophils were found. The remainder of the cutis was rather poor in cellular elements.

Psoriasis Vulgaris Treated with Hematoporphyrin. Presented by Dr. Henry Silver.

I. G., a man aged 27, single, states that he has suffered for the past eighteen years from an inveterate, therapy-resistant psoriasis. His father has psoriasis of the elbows. No other members of the family are affected. The patient has been treated by many dermatologists and at various clinics and has received ultraviolet and roentgen radiation and injections of autoblood, sodium gold thiosulfate and calcium. Recently he was put on a fat-free diet.

The patient came under observation in May 1932. At that time he presented lesions on the scalp and the trunk. The lesions were papular and scaly and on the trunk followed the lines of cleavage. The elbows and the knees were always free from eruption. Treatment with ultraviolet radiation in combination with tar ointment, as suggested by Goeckerman, and a series of injections of autoblood were of little benefit.

Three months ago the patient was operated on for an inguinal hernia on the left side. Soon after the operation the eruption became aggravated. Large, thick heavily scaled patches appeared on the sides of the chest and in the scar. The scalp was covered with scales.

Treatment with hematoporphyrin was instituted on Dec. 12, 1936. The patient first received ten intramuscular injections of 1 cc. of a solution of hematoporphyrin, followed by exposure to ultraviolet rays. After this course the patient was instructed to take hematoporphyrin by mouth in increasing doses. Two weeks later another course of injections was given and again followed by exposure to ultraviolet light. Marked improvement was noted. The thick patches began to clear in the center. The borders began to break up into individual papules, showing the reverse of the process of coalescence and formation of plaques. Many small lesions and patches healed completely.

DISCUSSION

Dr. Sidney B. Rooff (by invitation): The use of hematoporphyrin in the treatment of psoriasis is still in the experimental stage. Hematoporphyrin, which is an iron-free derivative of hemoglobin, has photosensitizing properties. In view of this, Dr. Silver suggested its use for psoriasis in combination with ultraviolet radiation. Seven patients were treated, and the patient presented is one of the group. The injections are given intramuscularly and immediately followed by exposure to ultraviolet rays. The results obtained warrant further trial of this method of therapy.

Dr. David Bloom: I hope that this treatment will prove successful, but I must point out that psoriasis is extremely capricious in its response to treatment. This may be shown by the following incident: A few years ago a patient with extensive psoriasis was under my observation at the Bellevue Hospital. A moulage was taken from lesions on the arm. A few days later the patient returned, praising the marvelous treatment he had received, for not only the eruption on the arm had improved, but also that on the rest of the body. This incident indicates the unpredictable behavior of psoriasis and the necessity for being extremely cautious about evaluating any kind of therapy.

Dr. Marion B. Sulzberger: I know that Dr. Silver knows as well as any of the members just how capricious psoriasis is. Regarding the use of ultraviolet rays in psoriasis, many patients get well during the summer when they are exposed more frequently to light; on the other hand, it should be noted that undoubtedly some few patients get much worse in the summer and improve in the winter. The use of photosensitizing agents for relief of psoriasis is not new. One of the medicaments used for this purpose is tar; another is fluorescein, and still another is porphyrin. I have just started using fluorescein in a few cases. Good results have been reported, but they have not yet been observed in my cases.

Dr. Henry Silver: The treatment with hematoporphyrin has been used with good results for patients with psychiatric conditions, particularly those with depressive psychoses. Hematoporphyrin interested me from another point of

view. I was familiar with the experiments with, and the enthusiastic reports on the use of, photosensitizing agents in treatment of psoriasis. Years ago Oppenheim used acriflavine hydrochloride intravenously in a series of cases and followed the treatment with exposure to ultraviolet radiation. The treatment was abandoned because of the marked pigmentation and yellowing of the skin. The recent use of fluorescein also gave encouraging results.

About half a dozen subjects were selected, mostly those whose condition was of the inveterate type and had resisted all forms of treatment, and treatment with hematoporphyrin was instituted. The drug is not innocuous, and care should be taken that the patient's cardiorenal system is in good condition. The psoriatic skin seems to tolerate the drug well, and no untoward reactions have been observed. The results obtained have not been spectacular. The drug has a definite cumulative effect, and several months must elapse before improvement is evident.

Acanthosis Nigricans, Associated with Carcinoma of the Stomach. Presented by DR. MARION B. SULZBERGER.

I. R., a pedler aged 63, born in Russia, was admitted to the Montefiore Hospital for Chronic Diseases on July 19, 1937. For more than fifteen years he has suffered from occasional swelling of both legs and ulcers on the right shin. He states that all cutaneous lesions except those on the legs appeared within the past three months. There were no symptoms referable to the gastrointestinal tract. The patient has lost 10 pounds (4.5 Kg.) since the onset of the eruption, 7 pounds (3.2 Kg.) of which he regained during a stay at the Bronx Hospital in December 1936.

The physical examination showed no abnormality except an enlargement of the liver to a point 2 fingerbreadths below the costal edge and a few subcutaneous nodules on the right side of the abdomen.

The skin in general is slightly thickened, and there is a yellowish brown discoloration of the entire integument. Numerous small soft fibromas are seen on the face. On the back of the neck there is a large area, extending toward both shoulders and scapulae, which shows marked brownish black pigmentation. There are numerous verrucous lesions which are smaller than a pinhead and do not leave any normal skin in between; in the same area the depth of the furrows in the skin is considerably increased. There is slight brown discoloration of the skin of both axillae. A few verrucous flat lesions the size of a lentil are seen on both forearms. The palms and soles are markedly hyperkeratotic. The nipples are much larger than normal and brownish black. On the back, in the lumbar region and on the forearms large, irregularly shaped rough black-brown areas are encountered. On both shins there are areas larger than a palm which show dirty brown patches in some parts and white sclerotic ones in others. In these areas the skin is thickened and cannot be lifted from its base. On the right shin there is a fairly deep ulcer the size of a 25 cent piece, the edge of which is hard and does not show any tendency toward healing. On the left shin there are many verrucous growths the size of a pinhead in the previously mentioned discolored area.

The course of the disease has been marked by fading of the lesions on the neck and the back. On Feb. 23, 1937, the patient complained for the first time of pain in the right side of the abdomen and marked tenderness was found in that region on palpation.

Histologic examination of a section taken from a lesion of the neck showed an irregular acanthosis of the epidermis. The irregular surface was covered by a loose horny layer. The basal cell layer showed marked pigmentation. The cutis showed nothing of note. The microscopic diagnosis corroborated the clinical diagnosis of acanthosis nigricans.

Histologic examination of the verrucous lesions on the leg showed a warty nodule covered by a stratified squamous epithelium, with considerable keratinization of the surface. The stroma was hyalinized and contained a few lymphocytes around the blood vessels. There was no evidence of amyloid.

The roentgen examination of the gastrointestinal tract showed a lesion on the lesser curvature of the stomach which was highly suggestive of malignancy.

Two determinations of the basal metabolic rate gave results of plus 34 and plus 42 per cent. The blood count revealed secondary anemia. The serologic and chemical examinations of the blood showed no abnormality. The congo red test showed 95 per cent of the dye left in the blood stream after one hour. The gastric analysis disclosed hypo-acidity and a poor response to histamine; blood was present in all specimens. The dextrose tolerance test showed a curve of 97, 166, 117, 94, 92 and 103 mg. per hundred cubic centimeters. The examination of the urine gave negative results. The examination of the stool showed the presence of blood. (The patient is under the care of Dr. R. Baer).

DISCUSSION

DR. MARION B. SULZBERGER: I should like to hear Dr. Curth discuss this case, as she recently published a paper on the connection between acanthosis nigricans and cancer (ARCH. DERMAT. & SYPH. **34**:353-366 [Sept.] 1936).

DR. HELEN O. CURTH (by invitation): I agree, of course, with Dr. Sulzberger's diagnosis of acanthosis nigricans. I was so much impressed by the occurrence of malignant growth in association with acanthosis nigricans that I began to look for cancer even in cases in which it was not suspected. This search revealed a history of cancer in the families of patients with so-called benign acanthosis nigricans. Certain facts lead me to believe that there is a genetic relationship between the two diseases. If this view is accepted, a few doubtful points become clear. One usually associates acanthosis nigricans with cancer in the abdominal cavity, but cancers located elsewhere, as in the breast and the lungs, are found associated with this condition. It is the glandular character of the cancer that is important, rather than its location.

The answer to the question as to which of the two diseases begins first varies, and cases are recorded in which acanthosis nigricans preceded the cancer by ten years or more. The answer really is not important if the two diseases are genetically related. Another important point is that the two types of acanthosis nigricans —histologically and clinically identical—have a common etiology if the theory of genetic relationship is accepted.

DR. ADOLPH ROSTENBERG: The presence of acanthosis nigricans is at times helpful in establishing the diagnosis of a malignant growth. In this connection the following incident is of interest: An elderly man, who suffered from some indefinite stomach complaint, presented typical acanthosis nigricans. Roentgenograms did not reveal carcinoma. I insisted that a malignant process must be present. A carcinoma of the stomach was found at autopsy.

Nodular Ulcerative Syphilis (Hereditary?). Presented by DR. G. D. ASTRACHAN.

P. M., a woman aged 22, of Italian parentage, born in the United States, was first seen on March 18, 1937, when she presented an eruption on the face of six months' duration. She states that she received injections in early childhood and that her father had a "blood disease." The mother died from cardiac disease at the age of 33. Tests of the husband's blood by a private physician gave negative results.

At the age of 4½ years the Wassermann reaction of the patient's blood was reported as 4 plus at the New York Post-Graduate Medical School and Hospital. The patient is in the seventh month of pregnancy.

On the lower part of the left nostril and involving the adjacent parts of the upper lip is a well defined irregular elevated lesion the size of a 5 cent piece. The border of the lesion is light brown and markedly infiltrated. The central portion is covered with a heavy dark grayish crust. There is a large elevated infiltrated brownish lesion the size of a pea on the left cheek. The septum shows a perforation, which appeared about two years ago after an operation on the nose. The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. G. D. ASTRACHAN: The question to be determined is whether this case is one of acquired or of prenatal syphilis. A Wassermann test made in 1920, when the patient was 4½ years old, at the New York Post-Graduate Hospital gave a reaction of 4 plus. It might well be that this case is one of syphilis acquired in infancy. More likely, the condition is nodular ulcerated syphilid in a patient with congenital syphilis. Another important question is that of treatment. The patient is in the seventh month of pregnancy. In order to give her at least ten injections of arsphenamine, which is the minimum for a patient with prenatal syphilis, it will be necessary to give these injections more often than once a week. In view of the facts, however, that the syphilis of the mother is of long duration and the prognosis for the baby is good, I do not believe that it is worth while to endanger the mother's health by giving her arsphenamine too often.

DR. ADOLPH ROSTENBERG: I think Dr. Astrachan ought to try to establish whether the patient is suffering from congenital syphilis or not. One should look for the stigmas of congenital syphilis. I cannot see why the patient should not have the full benefit of treatment, including as many as eight injections of arsphenamine, in order to safeguard the child. It is unusual to see tertiary manifestations in congenital syphilis at the patient's present age.

DR. CLINTON H. MARTIN: There is a definite nodular lesion in the left cheek. There is also an erythematous papular lesion on the right cheek and above this a deeply situated nodular lesion. These lesions may break through and scar the patient badly. Therefore, if the kidneys are normal, active treatment should be instituted at once.

DR. CHARLES WOLF: This patient is in the seventh month of pregnancy, and if the child is not stillborn it should show syphilitic lesions. I believe that antisyphilitic treatment at this stage would probably have little effect. It would be interesting to report at a future date whether or not there were any lesions of syphilis in the child at birth. I believe, however, in giving this patient vigorous antisyphilitic treatment, provided the kidneys are not affected. The patient is not congenitally syphilitic but probably acquired syphilis during early life.

DR. G. D. ASTRACHAN: It is difficult to prove definitely that this case is one of prenatal syphilis. In my opinion it is because syphilis is rarely acquired in infancy. I cannot agree with Dr. Wolf about the prognosis for the baby. This patient has syphilis of long standing, at least twenty years, and I think that the child will be born free from syphilis, especially if the mother receives treatment with arsphenamine.

Carcinoma of the Lower Lip Simulating Chancre. Presented by DR. CHARLES WOLF.

J. S., a man aged 47, has been a heavy smoker in the past but has not used any form of tobacco in the last two or three years. About eight weeks ago a small sore appeared on the left side of the lower lip; it grew rapidly and became ulcerated. The lesion is the size of a hazelnut, slightly elevated and infiltrated. There is an enlarged left submaxillary gland.

The Wassermann and dark field examinations gave negative results. The histologic examination showed a squamous cell carcinoma. The patient has received 275 millicurie hours of radon therapy, which resulted in softening of the lesion.

DISCUSSION

DR. WILBERT SACHS: Did the microscopic picture suggest an embryonic type of epithelioma? If there are numerous pearls and whorls present, then the patient's history is unreliable, and the lesion is not a highly malignant neoplasm. If that is true, I think that surgical procedure should be employed and followed by irradiation.

DR. LOUIS CHARGIN: While implantation of radium is an excellent method of therapy, I am in favor of surgical procedure for carcinoma of the lower lip, particularly in the presence of metastases to glands.

DR. FRANK E. CROSS: I saw this patient at a conference at the Mount Sinai Hospital and made a definite diagnosis of epithelioma. My diagnosis was later confirmed histologically. I think it would be advisable to remove a submental gland to determine whether metastases are present.

DR. ARTHUR SAYER: I believe that this type of tumor is best treated by interstitial irradiation, as suggested by Cade. He advocated that several needles containing small quantities of radium be implanted in the lesions and left for a long time (about five or six days), the total being about 150 milligram hours of treatment. This method has many advantages, since it leaves a fine scar and recurrences are less frequent. Shelmire also recently reported treating a series of surface squamous cell carcinomas by this method with excellent results.

DR. HARRY C. SAUNDERS (by invitation): I have treated several carcinomas of the lower lip in the manner just mentioned by Dr. Sayer, and the results were most satisfactory.

DR. CHARLES WOLF: The patient is receiving radium treatment in daily doses of 50 milligram hours and is showing rapid improvement. Dr. Paul Klemperer reported a typical squamous cell carcinoma. I intend to remove a biopsy specimen from the gland by aspiration and give prophylactic high voltage roentgen radiation.

Erythema Annulare Centrifugum (Darier). Presented by DR. PAUL GROSS.

C. P., an Italian woman aged 27, had infantile paralysis in childhood. The cutaneous lesions have persisted for the past ten years with remissions, an attack lasting from two to three weeks. The patient says she has not taken drugs. She admits, however, that she uses a weak solution of iodine for her frequent attacks of tonsillitis.

The lesions on the neck, the chest and the abdomen vary in size and in shape. The smallest are annular or papular; the largest are the size of a palm and show clearing of the centers with some faint hyperpigmentation. The borders, which are about 0.5 cm. wide, are brick red. The lesions are sharply outlined. Mild scaling is present between the center and the periphery in the larger lesions.

The microscopic examination for tinea and the Wassermann test of the blood gave negative results. The physical examination disclosed enlarged and infected tonsils. (The patient is under the care of Dr. Helen O. Curth.)

DISCUSSION

DR. MARION B. SULZBERGER: I am inclined to agree with the diagnosis if tinea cannot be demonstrated in these lesions. However, I think there is a form of superficial tinea which can mimic the lesions in this patient. The features in this case which are unusual for Darier's erythema centrifugum are the scaliness, the multiple sites and the lack of any urticarial element.

DR. ADOLH ROSTENBERG: There is a form of annular erythema described by Lipschütz which bears a closer resemblance to the condition here than does Darier's erythema annulare centrifugum.

DR. FRANK E. CROSS: This eruption has a bizarre circinate appearance with large circles, which one can see only in erythema annulare centrifugum. The border in tinea is more serpiginous and vesicular.

DR. SAMUEL M. PECK: The diagnosis of erythema annulare centrifugum is made less likely by the presence of large circular patches. Before the diagnosis of tinea is ruled out, additional scrapings and cultures should be made. The presence of scaling at the border speaks also against the diagnosis of erythema annulare centrifugum.

DR. MARION B. SULZBERGER: I know that this picture is not characteristic of superficial tinea, but I have observed cases in which there were rings as large as these and even much larger, and I was able to demonstrate fungi in them. In many of these cases the condition was due to Trichophyton purpureum.

Lichen Planus with Lesions of the Scalp. Presented by DR. ARTHUR SAYER.

R. B., a widow aged 60, born in Germany, came under observation on March 18, 1937, with an itching eruption of two weeks' duration on the trunk. The diffuse eruption, which involves the neck, the back and the forearms, consists of numerous slightly elevated flat-topped shiny violaceous papules the size of a pinhead. The eruption is typical of lichen planus. Lesions characteristic of lichen planus are also present on the dorsum of the tongue and on the buccal mucosa.

On the entire scalp there are diffusely scattered pinkish erythematous papules the size of a pinhead. These lesions do not show any of the usual characteristics of papules of lichen planus but show a tendency to arrangement in short linear groups. Marked alopecia, associated with atrophy of the skin on the scalp, has been present for the past ten years. It is probably the end-result of folliculitis decalvans.

The Wassermann test of the blood and examination of the urine gave negative results.

DISCUSSION

DR. CHARLES LERNER: None of the lesions on the scalp appeared to be characteristic of lichen planus. However, I agree with the presenter's diagnosis of lichen planus of all other parts of the body.

DR. ARTHUR SAYER: It is true that the lesions on the scalp do not have the violaceous color of lichen planus, nor are they flat topped or umbilicated; nevertheless, I cannot conceive of their being anything else but lichen planus. I consider this case interesting, because lesions of the scalp are uncommon in lichen planus.

Leprosy in Cuba (Demonstration of a Series of Lantern Slides). Presented by DR. ADOLPH ROSTENBERG.

DISCUSSION

DR. MARION B. SULZBERGER: The demonstration of slides by Dr. Rostenberg is instructive. It is interesting to note that at the leprosarium considered here there is no record of acquisition of leprosy by any of the personnel, and only ordinary precautions are used. For instance, the physicians do not live in the leprosarium at Rincon, Cuba. They go in and out to Havana every day, to their patients and their families. There is no fear that they will transmit leprosy in this way. Children are apparently much more susceptible than adults. There are from 3,000 to 5,000 lepers in Cuba, but only a few more than 300 are isolated in this lazaretto. About 60 per cent of the leper colony have had positive Wassermann reactions but negative Kahn reactions. I inquired about the incidence of positive Wassermann reactions in the ordinary population of Cuba, and it was said to be 10 per cent.

DR. FRANK E. CROSS: Dr. John A. Kolmer of Philadelphia insists that with the Kolmer modification of the Wassermann test only persons with syphilis or frambesia give positive reactions.

Book Reviews

Latent Syphilis and the Autonomic Nervous System. By Griffith Evans. Second edition. Price, $3. Pp. 158, with 50 illustrations. Baltimore: William Wood & Company, 1937.

In the opening chapter the author states the reasons for his belief in the lymphatic hypothesis and in McDonagh's hypothesis of a sporular stage in the life cycle of Spirochaeta pallida. Applying "this newer pathology of syphilis," he points out that structures such as the vagus nerve and the esophagus in the thorax "and the sympathetic ganglia in the abdomen can hardly escape so wide spread and destructive a process as the perilymphatic infiltration" described by the proponents of this theory.

On this pathologic basis he concludes that many obscure conditions which confront the general practitioner may be due to such an infiltration and may call for the consideration of latent syphilis in diagnosis. Among the diseases and symptoms calling for such considerations he includes some of the diseases of the thyroid gland, certain allergic conditions, asthma, vasomotor disturbances such as angioneurotic edema and purpura, nervous dysphagia, nervous dyspepsia, the "chronic abdomen," abdominal adhesions and pes cavus.

While he accepts as affirmative evidence the positive Wassermann test, the demonstration of the spirochetes and the presence of pathognomonic lesions, he rejects the absence of such indications as proof that syphilis is not present. In the absence of all three he is willing to diagnose as latent syphilis (either congenital or acquired) a large variety of conditions on evidence furnished by family or personal history or by isolated signs or symptoms. As proof he offers the histories of numerous cases in which there has been a response to specific medication with mercury, bismuth, the iodides and, in a few instances, arsenic. "This [response to specific therapy] is a very important criterion in diagnosis and is a much more important piece of evidence than any Wassermann test."

In only a comparatively few instances has examination of the spinal fluid been reported. A routine examination of this would undoubtedly have furnished much more orthodox evidence of the presence of syphilis.

In chapter XI there are instructive tabulations of the most frequent symptoms and the Wassermann reactions and clinical signs found in 100 consecutive cases of latent syphilis.

In chapter XIII there is an able and interesting discussion of the relation between syphilis and cancer. In appendix A the author tabulates symptoms in twenty-five cases of cancer suggesting an association with syphilis. In appendix B are a number of illustrations of histologic observations in syphilis and cancer.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102—2nd Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. J. McGovern, President, 4005 Dorchester St., Montreal.
F. L. Boulais, Secretary-Treasurer, 2061 St. Denis St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Joseph V. Klauder, Chairman, 1934 Spruce St., Philadelphia.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: San Francisco. Time: June 13-17, 1938.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: San Francisco. Time: June 1938.

American Dermatological Association

James Herbert Mitchell, President, 25 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Del Monte, Calif. Time: June 8-11, 1938.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: December 1937.

Mississippi Valley Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: St. Louis, Mo. Time: Dec. 4, 1937.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

Northern New Jersey Dermatological Society

Charles R. Mitchell, President, 311 Broadway, Paterson.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

Harry M. Robinson, Chairman, 106 E. Chase St., Baltimore, Md.
Winston U. Rutledge, Secretary, 332 W. Broadway, Louisville, Ky.
Place: New Orleans. Time: Nov. 30-Dec. 1-3, 1937.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson Paul Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.
Place: Pasadena. Time: May 9-12, 1938.

Connecticut State Medical Society, Section on Dermatology

E. Myles Standish, Chairman, 179 Allyn St., Hartford.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.
Place: New Haven. Time: May 19, 1938.

Florida Society of Dermatology and Syphilology

C. A. Andrews, Chairman, 706 Franklin St., Tampa.
Lauren Sompayrac, Secretary, 204 Laura St., Jacksonville.
Place: Jacksonville. Time: June 1938.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

George A. Dix, President, 6 Ashland St., Worcester.
J. Harper Blaisdell, Secretary, 45 Bay State Rd., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Mark Heiman, Secretary, 600 Medical Arts Bldg., Syracuse.

Medical Society of the State of Pennsylvania Section on Dermatology

L. G. Beinhauer, Chairman, 5026 Jenkins Arcade Bldg., Pittsburgh.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.
Place: Scranton. Time: October 1938.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

G. Warren Hyde, Chairman, 2501 W. Grand Blvd., Detroit.
Ruth Herrick, Secretary, 26 Sheldon Ave., Grand Rapids.
Place: Grand Rapids. Time: Sept. 27-30, 1937.

MINNESOTA DERMATOLOGICAL SOCIETY

John Madden, President, 350 St. Peter St., St. Paul.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Charles P. Bondurant, President, 412 Medical Arts Bldg., Oklahoma City.
Darrell G. Duncan, Secretary, 914 Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Bedford Shelmire, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Galveston. Time: May 9-12, 1938.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Herman E. Kittredge, President, 1835 Eye St., N. W., Washington, D. C.
J. Louis Sandler, Secretary, 1835 Eye St., N. W., Washington, D. C.
Place: Baltimore. Time: October 1937.

BRONX DERMATOLOGICAL SOCIETY

Theodore Rosenthal, President, 115 W. 86th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: June 1938.

BROOKLYN DERMATOLOGICAL SOCIETY

David L. Satenstein, President, 57 W. 57th St., New York.
M. Edward Goebel, Secretary, 842 Union St., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

I. J. Arnsson, President, 468 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: Jan. 11, 1938.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Mark Heiman, President, 713 E. Genesee St., Syracuse.
Rudolph Ruedemann Jr., Secretary-Treasurer, 256 State St., Albany.

CHICAGO DERMATOLOGICAL SOCIETY

Otto H. Foerster, President, 208 N. Wisconsin Ave., Milwaukee.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.
Place: Chicago. Time: Third Wednesday in January 1938.

CINCINNATI DERMATOLOGICAL SOCIETY

Leon Goldman, President, Doctors Bldg., Cincinnati.
George E. Clarke, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

Claude B. Norris, President, 244 Lincoln Ave., Youngstown, Ohio.
Clyde L. Cummer, Secretary, 1010 Hanna Bldg., Cleveland.
Place: Cleveland. Time: May 26, 1938.

Detroit Dermatological Society

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1938.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Andrew J. Gilmour, Chairman, 121 E. 60th St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.
Place: New York. Time: May 1938.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 450 Sherbrooke St., E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Louis Chargin, Chairman, 1 W. 85th St., New York.
Harry C. Saunders, Secretary, 159 W. 87th St., New York.

New York Dermatological Society

Eugene F. Traub, President, 140 E. 54th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln.

Philadelphia Dermatological Society

Frank C. Knowles, Chairman, 2035 Spruce St., Philadelphia.
Thomas Butterworth, Secretary, 411 Walnut St., Reading, Pa.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

A. Fisher, President, 530½–5th Ave., McKeesport, Pa.
Francis P. Kenney, Secretary, Westinghouse Bldg., Pittsburgh.

St. Louis Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

John M. Graves, President, 909 Hyde St., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland.
Place: San Francisco. Time: Third Friday of November 1937.